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BRITISH MEDICAL JOURNAL

JOURNAL OF THE BRITISH MEDICAL ASSOCIATION

SATURDAY MAY 19 1951

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY MAY 19 1951

DIET IN DIABETES

BY

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Despite the long recognition of diabetes as a clinical entity, no successful method of treating the disease existed until the nineteenth century, when Rollo and Bourchadat discovered independently the value of dietary restriction. The latter noted the disappearance of glycosuria in diabetics when food was scarce during the Siege of Paris, and applied that observation to the management of his patients. In the twentieth century, Frederick Allen's work (Allen, 1914, 1917, 1923 ; Allen and Sherrill, 1922) on undernutrition in experimental diabetes in dogs put the dietary treatment of diabetes on a more rational basis. The clinical results obtained by the use of restricted diets were good in the case of mild and obese diabetics, but among other diabetics deaths from diabetic coma and tuberculosis were very common. Pregnancy was an exceedingly rare occurrence, and diabetic children did not grow satisfactorily. The discovery of insulin by Banting and Best in 1921 revolutionized the treatment of the disease. Since its introduction the necessity for subcaloric diets, and indeed for dietary restriction of any kind, has become a matter of controversy.

Nobody questions the need for rigid dietary restriction for patients who are overweight, but for the diabetic who is not obese, and who requires insulin, three main types of dietary treatment are at present in use.

1. A strict regime, in which the calories and all the proximate principles are meticulously prescribed, and which aims at the maintenance of normal blood-sugar levels and of a practically sugar-free urine.
2. A more liberal method, involving the regulation of only the carbohydrate and total calorie intake, but allowing mild hyperglycaemia and glycosuria in order to prevent frequent insulin reactions.
3. A "free" diet, in which hyperglycaemia and glycosuria are disregarded, and in which the criteria of adequate insulin treatment are freedom from hunger, thirst, pruritus, nocturia, and ketosis, and the maintenance of weight and energy on the one hand, and the avoidance of hypoglycaemic symptoms on the other.

Such a diet, free of any restriction or regulation of food intake, was first advocated by Stolte (1931). It has been used by many physicians, including Lichtenstein (1938, 1945), Tolstoi and Weber (1939, 1940), Tolstoi, Almy, and Toscani (1942), Tolstoi (1943), and Micks (1943, 1944), and adopted independently by many patients. The most important advantage claimed for this form of treatment is the psychological benefit obtained through freedom from irksome regulations. Diabetes is a chronic disease, at present incurable, and to minimize its hardships the fewer the restrictions imposed upon the patient's daily life the better. The advocates of "free" diets reason that if insulin is required at all it does not matter very much to the patient whether the dose is 30 or 50 units a day, whereas it does matter to him a great deal that he should be able to take a normal diet—"that" (as a diabetic doctor has said) "each meal should be an elegant satisfaction of appetite rather than a problem in arithmetic and a trial of self-abnegation" (*Practitioner*, 1946). They claim, too, that their patients are fully nourished and therefore more resistant to infections, including tuberculosis; that in children growth and sexual development are satisfactory; and that the incidence of pregnancy is high.

On the other hand, there are many who object that the use of liberal diets results in difficulty in clinical control; that frequent insulin reactions alternate with thirst, polyuria, and pruritus, associated with hyperglycaemia, glycosuria, and ketosis; that excessively large doses of insulin are required; that the patients become obese; and that degenerative complications occur earlier and more often.

This paper describes the study of a group of diabetics given a "free" diet over a period of five years.

Selection of Patients

Fifty patients were studied, of whom approximately one-half were newly discovered diabetics who had never been treated, and the other half patients who had been given dietary instructions at some time, but who were making no effort to adhere to them. Naturally the latter group included a number of rebellious spirits and a few people of subnormal intelligence. Obesity was the only bar to selection; as a result, the proportion of male patients included in the survey was unusually high. There were 34 males and 16 females. Their ages ranged from 9 to 71 years, and their occupations from sedentary work to heavy labouring.

A control group of 40 diabetics of comparable age and sex were chosen from out-patients attending the

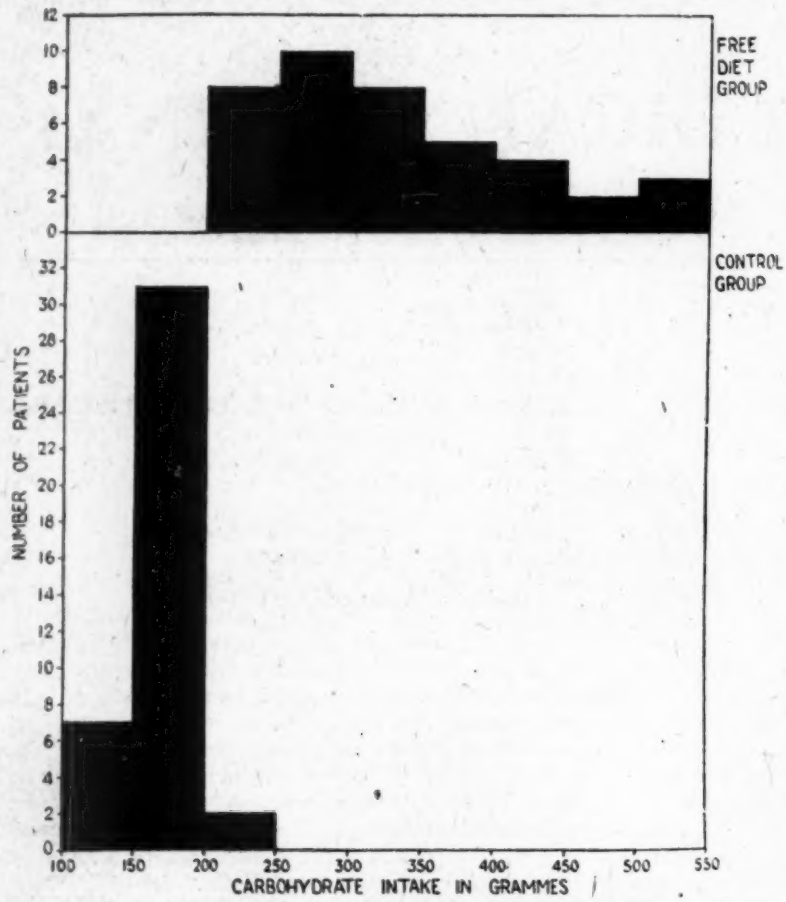

FIG. 1.—The daily carbohydrate intake of the "free diet" group and the control group.

Dietetic Clinic of the Royal Infirmary, Edinburgh. Only those who were adhering strictly to their diets and who required insulin were selected. Their diabetes was as well stabilized as could be expected of co-operative patients attending a busy centre. None of the patients in either group was suffering from any obvious diabetic complication or other disease at the time of selection.

In the charts that follow, the number of patients studied varies. This is not the result of deliberate selection, but of difficulties in the collection of data which are inseparable from clinical research on out-patients.

Method of Treatment

Patients who were taking a "free" diet were permitted to eat as their appetites dictated except for the omission of table sugar, jam, chocolates, and sweets, with the object of avoiding wild fluctuations of carbohydrate intake. During the period of study the British rationing system allowed all diabetics extra meat, bacon, milk, cheese, and fats. Thus the patients' standard of nutrition was probably higher than that of the general population.

Every patient received insulin once or twice a day. A simple powder method of testing the urine for acetone was used by the patients twice weekly on an early morning sample of urine, and every day during intercurrent infections. It was the rule to report any positive tests to the clinic immediately. Testing for sugar was not encouraged, as glycosuria was to be expected.

Patients visited the clinic, on an average, once a month, but were seen more often during the course of infections or other emergencies. At every visit the weight was checked and any positive acetone tests, insulin reactions, nocturia, or other symptoms were recorded. The dose of insulin was adjusted from time to time to maintain an adequate weight and freedom from either diabetic or hypoglycaemic symptoms. On each occasion a quantitative analysis was made of the sugar content of two samples of urine: (1) a morning specimen passed twenty minutes after emptying the bladder on rising, before food or insulin had been taken; and (2) a 24-hour specimen. The collection was made on the previous day and the quantity measured in pints by the patient. A small sample of this collection was brought for examination. Though the results of these urine analyses for sugar were useful for our purposes, they were not used to regulate treatment. Changes in insulin dosage were dictated solely by the patient's weight and symptoms or by the development of ketonuria.

Diets

Most patients took three main meals in the day, with a snack in the morning and again in the evening before going to bed. Co-operative patients whose accuracy could be trusted were asked from time to time to keep a written record of everything they ate or drank over

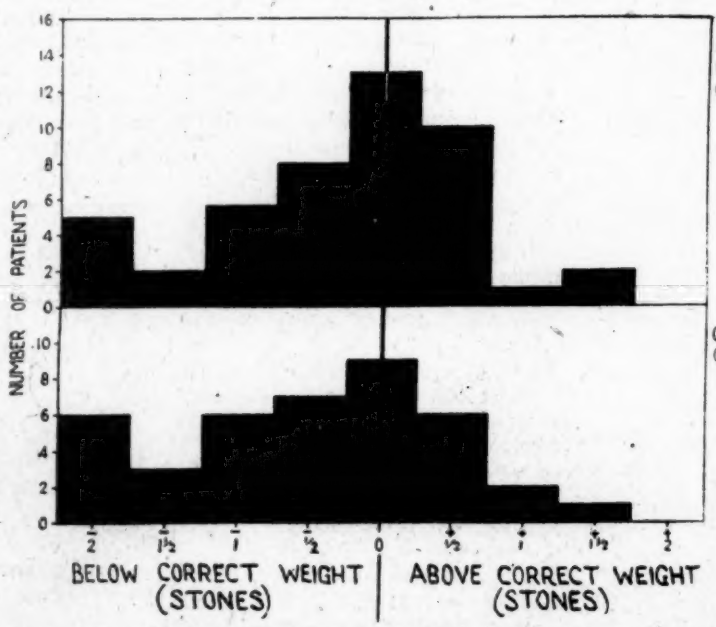

FIG. 2.—The relation of the present weights of the patients in both groups to their "correct" weights.

a period of one week. These records were discussed in detail with the patients, and it was felt that a reasonably accurate assessment of their diets was thus obtained. Analysis showed that the diets of the controlled group were higher in fat, much lower in carbohydrate, and somewhat lower in total calorie value than those of the group taking a "free" diet. Fig. 1 shows that the carbohydrate intake was considerably higher on a "free" diet than on the diets taken by the control group.

The carbohydrate intake on a "free" diet remained remarkably constant from one week-day to another, but rose or fell significantly at the week-end. The heavy labourer enjoying a lazy week-end was not so hungry, whereas the sedentary worker who played games ate more.

The carbohydrate intake of patients given a "free" diet from the time that their diabetes was diagnosed did not differ significantly from that of patients who had lapsed from a strict dietary regime. This eliminated the possibility that members of the latter group were unconsciously following dietetic instructions given in the past.

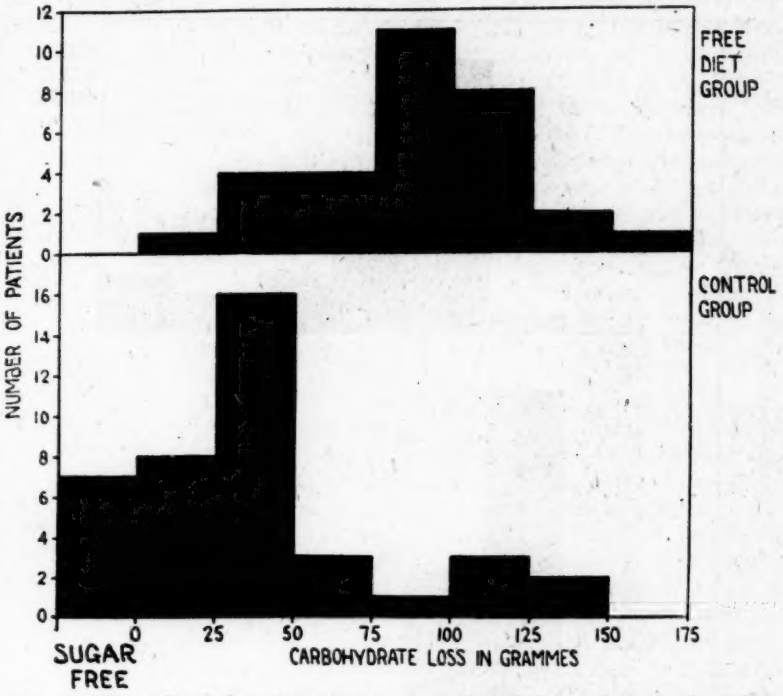

FIG. 4.—The daily carbohydrate loss in the urine of the patients in the "free diet" and control groups

Weights

If the criticism often levelled at the use of "free" diets, that many of the patients become obese, were true, it would constitute a grave objection to this form of treatment.

Fig. 2 compares the present weights of the patients after some five years of treatment with their "correct" weights. The distribution is remarkably similar for the two groups, there being no increased tendency for those taking a "free" diet to become obese. The patients who did become overweight on a "free" diet all gave a history of obesity in the past, though as a result of uncontrolled diabetes they were of normal or subnormal weight when they appeared for treatment.

Fig. 3 shows the relation of the patients' present weights to their "average" weights—that is, the weights which they maintained before the onset of diabetes. It is clear that the tendency of patients taking a "free" diet to revert to their pre-diabetic weight held not only for those who were previously obese but for the group as a whole. Dietetically controlled patients, on the other hand, tended to remain below their pre-diabetic weight.

If, as is generally agreed, a normal weight is the therapeutic ideal, patients who give a history of obesity before the onset of diabetes, even if they are thin by the time they appear for treatment, should be given controlled diets. Those who have never been overweight may be given full diets without much danger of their becoming obese.

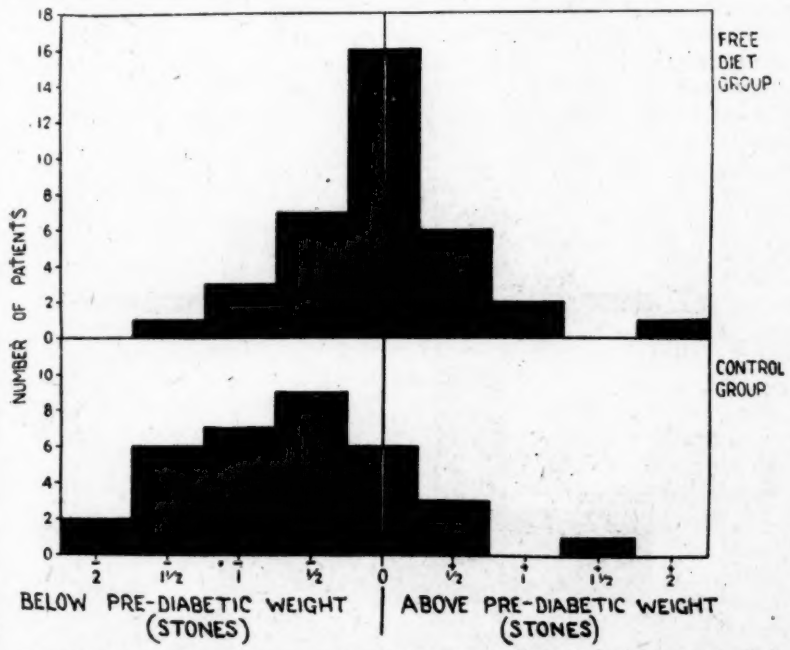
FREE DIET GROUP
CONTROL GROUP
NUMBER OF PATIENTS
2 1½ 1 ½ 0 ½ 1 1½ 2
BELOW PRE-DIABETIC WEIGHT (STONES)
ABOVE PRE-DIABETIC WEIGHT (STONES)

FIG. 3.—The relation of the present weights of the patients in both groups to their pre-diabetic weights.

Urine-sugar Studies

The accurate collection, once a month for six consecutive months, of the urine passed during the 24-hour period of a working day demands the full co-operation of the patient. Only those who could be relied upon to be accurate are included. The results shown in Figs. 4 and 5 are based on an average of the sugar content of six 24-hour samples. Meal charts covering the 24-hour periods during which the urine collections were made were brought with each specimen.

The average daily carbohydrate loss in the urine was greater in the "free diet" group than in the control group

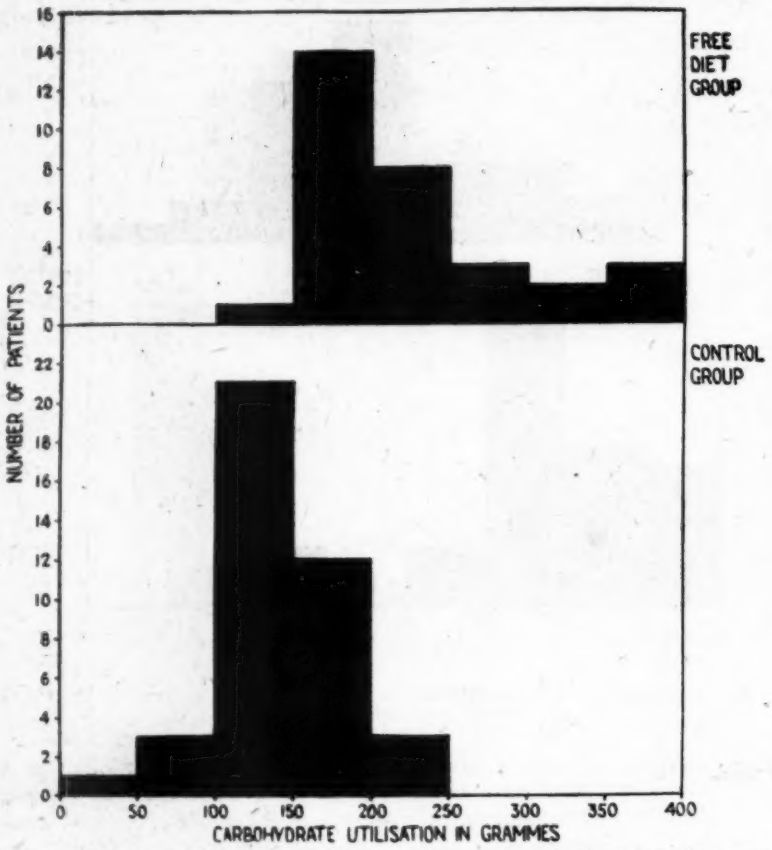

FIG. 5.—The daily carbohydrate utilization of the patients in the "free diet" and control groups.

by 50 to 75 g. (Fig. 4). In spite of this (Fig. 5) their total daily carbohydrate utilization was greater by at least 50 g. because of their higher carbohydrate intake. It is evident, therefore, that the quantity of carbohydrate metabolized by these patients on a "free" diet was adequate.

Blood-sugar Studies

Information about blood-sugar levels was obtained by taking blood samples from co-operative members of both groups in their homes or places of work during a normal day. The samples were taken before breakfast, lunch, and the evening meal. A fasting period of at least two hours preceded the withdrawal of blood. The highest of these three blood-sugar recordings was used in constructing Fig. 6, which shows that a higher proportion of patients on a "free" diet exhibited hyperglycaemia and that the degree of hyperglycaemia was greater than in the case of the control group. However, more than half of the patients in the latter group had blood sugars above 200 mg. per 100 ml. before a meal, illustrating how difficult it is to attain the ideal of normoglycaemia even when postprandial rises in blood sugar are discounted.

The lowest blood sugars were similar in the two groups. From these findings it follows that the fluctuation of blood-sugar level during the course of the day was greater in the group of patients taking a "free" diet.

Clinical Control

Eleven of the original 50 patients given a "free" diet could not be satisfactorily controlled with this form of treatment. They are considered in detail below. By adjusting their insulin dosage from time to time no difficulty was experienced in keeping the remaining 39 patients free from hunger, thirst, pruritus, and nocturia. Ketonuria was only an occasional finding during the course of intercurrent infections. The frequency of minor insulin reactions was not appreciably higher than among dietetically controlled patients. Like all diabetics, most of the patients experienced mild reactions from time to time, which were readily alleviated by taking a lump of sugar. (Hypoglycaemic coma is considered later.) The patients maintained an adequate weight and full physical energy. They seemed happy, and had a balanced outlook on their disease. Intercurrent infections did not appear to be commoner than among the control group.

The incidence of pregnancy was high. Seven of the eight married women in the child-bearing age became pregnant, one woman twice during the period studied. Of the eight babies, six are alive and two were stillborn. It has been noted that a high proportion of the women reporting to the Diabetic Pregnancy Clinic were taking a diet of normal calorie value at the time of conception, either because they belonged to the "free diet" group or because they had defaulted from their dietetic instructions.

There were seven young people in the "free diet" group of patients. Three were girls of 16 in whom menstruation had begun before the onset of diabetes, and who had stopped growing. The other four were boys of 15 or under in whom further growth was to be expected. Details of their rate of growth are given in Table I. It is significant that growth, which had been unusually rapid before the onset of diabetes, continued

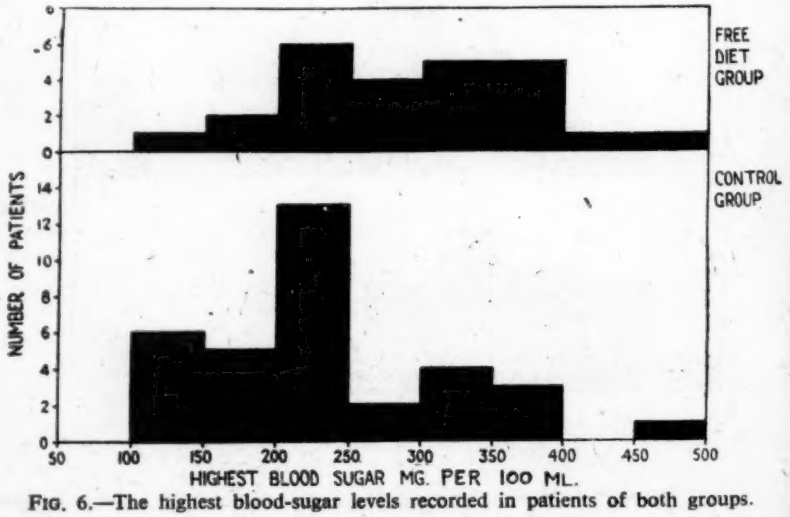

FIG. 6.—The highest blood-sugar levels recorded in patients of both groups.

at an excessive rate while they were taking a "free" diet.

TABLE I.

Case	Age at End of "Free Diet" Treatment	Duration of "Free Diet" Treatment	Increase in Height During Treatment	Normal Increase in Height for Same Period
1	11 years	2 years	4·5 in. (11·4 cm.)	3·8 in. (9·7 cm.)
2	17 ,,	3 ,,	7·5 in. (19·1 cm.)	4·6 in. (11·7 cm.)
3	16 ,,	2 ,,	6·5 in. (16·5 cm.)	3·2 in. (8·1 cm.)
4	15½ ,,	½ year	1·5 in. (3·8 cm.)	0·8 in. (2·0 cm.)

Normal height increments are taken from the table on page 290 of *Endocrine Disorders in Children and Adolescents*, by Le Marquand and Tozer, London, 1943.

Coma

Among the 50 patients on a "free" diet observed over five years three incidents of diabetic coma and seven of hypoglycaemic coma occurred. This contrasts with five incidents of diabetic coma and four of hypoglycaemic coma among the 40 patients in the control group. The incidence of hypoglycaemic coma is a little higher in the "free diet" group, and perhaps reflects the greater risk which attends an unregulated food intake and large doses of insulin.

Insulin

The type of insulin required and the number and timing of the injections varied from patient to patient. The majority were stabilized on an injection of soluble insulin and one of zinc-protamine insulin half an hour before breakfast, and a second dose of soluble insulin half an hour before the evening meal: 40 of the 50 patients required two injections a day.

TABLE II.

Total No. of Patients	No. Requiring More Insulin	No. Requiring Less Insulin	No. Requiring the Same Dose
47	20	4	23

Table II shows the changes in insulin requirement of the patients on a "free" diet. The dose required after five years' treatment or in the case of the 11 failures at the time of changing to a controlled diet is compared with the dose needed three months after beginning this form of treatment. The insulin requirement was considered to be unchanged if the rise or fall did not exceed 20% of the original dose. Only 47 patients are included in the table, as three defaulted from the clinic. The insulin requirement of the group as a whole has tended to rise during treatment. The most striking increases occurred in children of puberty age and young adults. Whether this trend will continue, making further changes to controlled diets necessary, is as yet uncertain.

Repeated blood-sugar curves were obtained in one-third of the patients in an attempt to assess whether the diabetic state was becoming milder or more severe under "free diet" treatment. In general, the results obtained agreed with the trend shown by the comparative insulin requirements—namely, an apparent increase in severity.

Complications and Failures

Miscellaneous illnesses, including pneumonia, cystitis, and infective hepatitis, occurred in a few patients, but only complications known to be associated with diabetes are considered in detail.

No patient in the group has so far developed peripheral arteriosclerosis, hypertension, or albuminuria. Two patients have suffered temporarily from diabetic neuropathy. Diabetic retinopathy has developed in four patients, and senile cataract in one. It is interesting to note that one young man developed diabetic retinopathy at the age of 28, only one year after becoming diabetic. It was definitely known that he had not been suffering from diabetes previously. In contrast, two patients who had never paid any attention to dieting since the onset of the disease showed no sign of degenerative complications after a duration of diabetes of 23 years in the case of a woman who is now 27, and of 25 years in the case of a man now aged 45.

During the course of this five-year survey 11 patients have had to be changed from "free" diets to regulated diets. In seven of them the diabetic state became too severe to be satisfactorily controlled with a total daily dose of 80 units of insulin. It was considered unjustifiable to raise this dosage further. Five of the seven were children and two were young adults. With regard to the other four, frequent insulin reactions made it essential to regulate the diets of one adult and one child; and two women were given subcalorie diets because they became obese and began to suffer from pruritus vulvae. Both had been overweight before the onset of diabetes. After the change to a restricted diet the two obese women improved immediately. Of the two patients in whom frequent insulin reactions dictated the change, one improved; the other, a child, remained liable to frequent hypoglycaemic attacks. There was a considerable fall in the insulin requirement of the seven patients who had been uncontrollable while taking 80 units a day on a "free" diet. A close study of the growth curves of the growing children revealed that the very rapid growth which took place while they were on a "free" diet was not maintained after the change to a more restricted regime, though the rate was still satisfactory.

Discussion

From our experience of a group of 50 diabetics given liberal diets and insulin over a period of five years we are satisfied that, if adolescents and obese diabetics are excluded, clinical control, as defined earlier in this paper, can be attained in most patients. However, the degree of hyperglycaemia and glycosuria and the daily fluctuation of blood-sugar levels are undoubtedly greater in such patients than in those on controlled diets.

Those diabetics whose insulin requirements gradually rose while taking the "free" diet until 80 units were required daily showed an increased liability to ketosis when infections supervened. Moreover, the danger of insulin reactions was increased roughly in proportion to the dose of insulin employed. We feel, therefore, that it is unjustifiable to keep patients on a "free" diet when such large doses are needed for clinical control. Seven patients have had to be changed to controlled diets for this reason, and the change will almost certainly be necessary for two other patients in the near future. Of these nine, five are adolescent children and the remaining four are young adults between the ages of 20 and 35.

The need for dietary restriction has become apparent after periods on liberal diets ranging from six months to five years. Fortunately, when a change over to a controlled diet has been made the insulin requirement has shown a considerable fall, and no permanent ill

effect has been observed. It is uncertain whether increasing insulin requirements may make dietary restriction necessary for other patients in years to come, but the fact that failures are still appearing after five years' treatment is disquieting. Results with non-obese patients aged over 35 have been uniformly good, and it may well be that it is for this group of diabetics that "free" diets will have their greatest value.

There are many physicians who believe that continued hyperglycaemia increases the severity of the diabetic state, and that if it is prolonged the development of the degenerative complications of diabetes is facilitated. However, a normal blood-sugar concentration may exist when subcalorie diets are used in the presence of inadequate quantities of liver and muscle glycogen, while hyperglycaemia by no means necessarily implies inadequate stores unless there is an associated ketosis. Indeed, Peters and Van Slyke (1931) defined diabetes mellitus as an inability to store glycogen, and made no mention of hyperglycaemia. It is important to distinguish hyperglycaemia which is endogenous in origin, due to breakdown of glycogen stores and tissue protein —an expression of poor carbohydrate utilization and usually accompanied by ketosis—from hyperglycaemia of exogenous origin resulting from an abundant carbohydrate intake, with which, however, carbohydrate utilization as the result of insulin therapy is adequate and there is no associated ketosis. This distinction is rarely made, and the evil effects of uncontrolled diabetes are often attributed to the hyperglycaemia rather than to the poor utilization of carbohydrate. No one questions the undesirability of hyperglycaemia of endogenous origin, but considerable controversy exists on the harmfulness of exogenous hyperglycaemia.

It thus becomes important to inquire into the relationship of hyperglycaemia to the pathological physiology of diabetes. The production of diabetes by pancreatectomy in the laboratory of von Mering and Minkowski (1889), and the discovery of insulin with its dramatic therapeutic properties, placed the pancreas in the forefront of diabetic pathology. In 1922 Allen and Sherrill demonstrated that the pathological changes in the β-cells of the islets of Langerhans caused by partial pancreatectomy in dogs could be accentuated by giving the animals high-calorie diets. Further, Dohan and Lukens (1947) reported that normal cats could be made diabetic when a sustained hyperglycaemia was induced by repeated intraperitoneal injections of glucose. There is thus ample evidence that in experimental animals the insulin-producing cells of the pancreas can be damaged by hyperglycaemia.

In man, however, diabetes cannot be considered purely as a disease of the pancreas. In the first place, a histologically normal pancreas is found at necropsy in a considerable proportion of diabetics (Warren, 1930), and, furthermore, the complete removal of the human pancreas causes a relatively mild form of diabetes, readily controlled by not more than 40 units of insulin a day (Ricketts, 1947), rather than the grave metabolic disorder often seen in the spontaneously occurring disease, for the control of which much larger doses of insulin may be required. It seems certain that in human diabetes, at least in its severer forms, other endocrine glands are involved. Animal experiments have shown the importance of the anterior pituitary gland and of the suprarenal cortex in the pathology of the disorder.

Houssay (1936) discovered that depancreatized dogs lived longer if the anterior pituitary was also removed. The reverse of this—namely, that permanent diabetes could result from continued injections of anterior pituitary extracts in adult dogs—was demonstrated by Young (1937). Along similar lines, Long and Lukens (1934) found that adrenalectomy ameliorated pancreatic diabetes in the cat, and Long and his co-workers (1940) and Ingle (1940) demonstrated the aggravation of the diabetes of partially depancreatized rats by the administration of certain fractions of suprarenal cortical extract. Further support is provided by clinical evidence : the occurrence of diabetes in association with acromegaly and Cushing's syndrome ; and the striking fall in insulin requirement which occurs in the rare event of the development of Addison's disease in a diabetic.

However, in most cases of diabetes in man it is uncertain to what extent the syndrome is due to failure of insulin production by the pancreas, and to what extent to an abnormal inhibition of the action of insulin by the anterior pituitary and cortical hormones. The effect of low-calorie diets in lessening the severity of human diabetes is an undoubted clinical fact, demonstrated on a large scale in the countries of Western Europe during the German occupation, but we do not know whether it is the result of "sparing" the pancreas or of inhibiting anterior pituitary function.

Jacobs (1948) showed that prisoners of war who had been suffering from prolonged undernutrition presented many of the features of anterior pituitary depression ; and it is well known that the clinical picture of advanced anorexia nervosa is in many respects indistinguishable from Simmonds's disease. Any attempt to alleviate diabetes by depressing the secretion of the "diabetogenic" hormone of the anterior pituitary, however, must lead to simultaneous suppression of the growth, thyrotrophic, corticotrophic, and gonadotrophic hormones. Indeed, the recent work of Young *et al.* (1949) has strongly suggested that, at least in animals, the growth and "diabetogenic" hormones are identical. From clinical observations Lawrence (1949) has formed the concept of "total diabetes." He believes that such a state is reached by most young diabetics within three years of the onset of their disease. Their daily insulin requirement becomes stable at between 40 and 60 units. His interpretation of this state is a final cessation of insulin secretion by the pancreas. If this view is correct the steadily rising insulin requirement of some young diabetics cannot be attributed to further depression of insulin secretion, but must be due rather to inhibition of injected insulin by pituitary or suprarenal cortical hormones.

The rapid growth, advanced bone age, and precocious dental development of children at the onset of diabetes (White, 1946) are generally regarded as expressions of overactivity of the anterior pituitary gland. It is significant that in our group of patients the children at the age of puberty maintained an accelerated growth while taking a "free" diet, and also showed the most striking increase in insulin requirement. Further, these tendencies were not maintained after a change to a controlled diet had been made. It is possible that the underlying pituitary overactivity of these children was perpetuated by the metabolic stimulus of a high calorie intake. The same mechanism may be responsible for the apparent worsening of the diabetic state of some of the young adult patients, and for the high incidence of pregnancy.

If this view is accepted, it follows that, for the young diabetic at least, a diet which is generous enough to allow for adequate growth and sexual function will to some extent result in stimulation of the anterior pituitary gland and a consequent worsening of the diabetic state.

Opinion is conflicting about the relationship of hyperglycaemia to peripheral vascular disease. Joslin (1947), as a result of his vast experience, is convinced that the meticulously controlled patient is "the one in best condition" after 20 years of diabetes. White and Waskow (1948), in a review of 350 young adults who had been diabetic for at least 20 years, showed that there was a correlation between the severity of vascular disease on the one hand and *poor diabetic control*, as shown by hepatomegaly, incidence of diabetic coma, hypercholesterolaemia, and hyperglycaemia, on the other. The longest follow-up of a group of patients taking a "free" diet, by Lichtenstein, indicated that the incidence of degenerative complications after 10 years' treatment was not unduly high, but even this period of observation is too short for a reliable assessment to be made. Dolger (1947), who observed 200 diabetics over a period of 25 years, found that vascular disease occurred neither sooner nor more frequently in patients with persistent glycosuria than in those whose urine was kept sugar-free. He believed that complications occurred more often in the older patients, and that the duration of the disease was the most important factor. A similar conclusion was reached by Goodof (1945) in relation to the characteristic renal lesion of diabetes first described by Kimmelstiel and Wilson (1936). As for diabetic retinopathy, Ballantyne (1946) stated: "The outstanding paradox is the lack of any apparent relation between the severity of the diabetes, the control of the condition by treatment, and the presence or absence of retinal changes." Ballantyne's opinion is endorsed by Wagener (1945) and by Croom and Scott (1949).

Rundles (1945) gave a detailed report of his observations in 125 cases of diabetic neuropathy. He found that in most instances neuropathy followed a long period of grossly neglected diabetic management associated with hyperglycaemia, thirst, polyuria, and loss of weight.

While the correlation between the development of some of the degenerative complications of diabetes and poor control of the disease is at least suggestive, no one has yet produced evidence that hyperglycaemia, accompanied by adequate carbohydrate utilization and good clinical control, is responsible for the development of vascular complications. The present survey can make no contribution to the solution of this problem, as five years is too short a period on which to base conclusions.

Summary

An investigation of the use of a "free" diet in the treatment of 50 diabetics over a period of five years is described. For comparison, 40 dietetically controlled patients were observed over the same period.

Clinical control, as defined in the paper, was achieved in 39 of the 50 patients. Though hyperglycaemia and glycosuria were the rule, carbohydrate utilization was satisfactory. The incidence of pregnancy was high, and the growth of the children was unusually rapid.

Results were uniformly good in patients over the age of 35, but the insulin requirement of the younger patients tended to rise. Five children and two young adults showed a progressive worsening of their diabetic state, and had to be given controlled diets for this reason. The change was also necessary for two patients who suffered from frequent insulin reactions, and for two others who became obese and developed pruritus. Only those patients who gave a history of obesity before the onset of diabetes became overweight while taking a "free" diet. There were three episodes of diabetic coma and seven of hypoglycaemic coma among the 50 patients during the five-year period of study; these did not vary very significantly from similar incidents among the controlled group.

The relationship of hyperglycaemia to the pathological physiology of diabetes and to the development of degenerative vascular complications is discussed. A distinction is made between "exogenous" hyperglycaemia, which accompanies a high carbohydrate intake in patients whose carbohydrate utilization is adequate, and "endogenous" hyperglycaemia, which results from breakdown of glycogen stores and tissue protein in association with poor control of the disease.

While there is no evidence that "exogenous" hyperglycaemia is the cause of degenerative complications, there is reason to believe that the high-calorie diets with which it is associated may be responsible for increasing the severity of the diabetic state in children and young adults. A possible mechanism of this action is suggested.

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On May Day, 1950, the Archbishop of Canterbury inaugurated a festival at the Mayday Hospital, Croydon, and this year it was again celebrated. The patients were visited in the wards by civic, ecclesiastical, and other guests, and then a service was held in the hospital chapel. Afterwards there was a staff tea at which the hospital committee, doctors, nurses, and guests mingled in an informal manner. Many old members of the staff returned to the hospital to mark the occasion, and the day's events were rounded off by a social evening organized by the hospital sports clubs.

"PRISCOL" IN TREATMENT OF PERIPHERAL VASCULAR DISEASE

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The pharmacology of 2-benzyl-4,5-imidazoline hydrochloride ("priscol") has been fully worked out in animals (Ahlquist *et al.*, 1947). It has complex actions, consisting of effects resembling the sympatheticomimetic amines, histamine and acetylcholine-like properties, and sympatholytic effects. These workers found that priscol produced peripheral vasodilatation, cardiac stimulation, and increased cardiac output in cats and dogs. Coronary vasoconstriction, bradycardia, increase in blood pressure, and stimulation of the gut were produced in rabbits. The last effect could be prevented by atropine. In addition, the administration of adrenaline after priscol caused general vasodilatation, suggesting reversal of adrenaline action.

Grimson *et al.* (1948a) conducted clinical trials with priscol on 43 patients with peripheral vascular disease, including 6 with Raynaud's disease, 15 with atherosclerosis obliterans, and 6 with thrombo-angiitis obliterans. The results in Raynaud's disease were satisfactory and improvement was effected in the atherosclerotic and thrombo-angiitis groups. The peripheral skin temperature of the lower extremities was increased five minutes after intravenous and 45 minutes after oral administration. Definite cutaneous vasodilatation resulted even after oral priscol, but in five cases oscillometric readings were not altered. Eleven patients with hypertension were treated, but the blood pressure fell in only four. In three patients cardiac output was measured, but the results were equivocal. In another series, 17 hypertensive patients were treated, 12 showing a fall in blood pressure (Grimson *et al.*, 1948b).

Rogers (1949a), using skin temperature and oscillometric methods of assessment, obtained similar results in 27 patients suffering from various forms of peripheral vascular disease, using 100 mg. of priscol daily by mouth. In a further observation of 15 arteriosclerotic patients between the ages of 46 and 79 years, Rogers (1949b) reported subjective and objective improvement with oral priscol. He noted that the blood pressure may increase.

Douthwaite and Finnegan (1950) found priscol to have a more lasting vasodilator effect than the commonly used vasodilators, and noted a selective affinity for the smaller arteries of the hands and toes. In nine patients with Raynaud's disease they obtained excellent results, and produced improvement in 24 patients who had claudication of arteriosclerotic origin. Side-effects were particularly common, even with oral administration. Lynn (1950) found that priscol acted mainly on the skin vessels, producing vasodilatation. After intravenous injections of 50 mg. the blood flow was increased in the hands and feet in 11 cases of Raynaud's phenomenon and in the feet in 17 cases with occlusive vascular disease. In the sympathectomized limb intravenous injection had no effect, but when priscol was given intra-arterially the blood flow increased locally, suggesting a direct action on the arterial wall. Intra-arterial injection also doubled the calf flow in the non-sympathectomized limb. The results of oral treatment in the spastic group were good, but little or no improvement was noted in the occlusive group with claudication.

Side-effects have been reported, particularly after parenteral administration. These include faintness, vertigo, headache, sweating, and "goose-flesh." The blood pressure may rise, fall, or remain unaltered. Two of Grimson's patients had myocardial infarcts while taking the drug.

Present Investigation

In view of the lack of effective therapeutic agents for the ambulant treatment of patients with peripheral vascular disease, we decided to investigate the effects of oral priscol. The advantages of an effective oral preparation are obvious, particularly as other medical treatment has often very little to offer.

Twelve patients between the ages of 47 and 75 years with obliterative vascular disease were studied. The series included seven patients with hypertension, three of whom had previously suffered from coronary occlusion, which in two cases had probably resulted in aortic "saddle" emboli. Another hypertensive patient had mitral stenosis, auricular fibrillation, and multiple femoro-popliteal emboli.

The effect of priscol was assessed objectively by means of skin temperature readings, reflex heating tests, and measurement of circulation rate using sodium fluorescein. Arteriography was performed on suitable cases.

Reflex Heating

The patient lay on a couch in a cool room (temperature 19–21° C.), and skin temperature readings were taken with a "Light" multichannel skin thermometer. One channel was attached to the pulp of each great toe and each mid-calf region by means of adhesive plaster. After the resting temperatures had become stabilized, control readings were taken. The patient's trunk was then heated by means of an electric blanket at a temperature of 60° C. for one to one and a half hours, until the skin temperature readings showed no further increase. The room temperature was kept at 19–21° C., for separate observations and during each observation. In all cases the toes were cooler than the calves before heating. After heating, both toe and calf temperatures increased, the former to a greater degree than the latter. Thus reflex heating produced a reduction in the toe–calf temperature difference, or gradient. As a result of the response to reflex heating, the patients were placed in two groups.

Group I (spastic-occlusive) comprised those patients in whom the toe–calf temperature gradient was significantly reduced or abolished by reflex heating, suggesting that they had a considerable number of collateral vessels capable of dilating in addition to vessels grossly narrowed by the pathological process.

Group II (occlusive) was formed by those patients in whom the toe temperatures did not rise enough after reflex heating to reduce the toe–calf gradient so significantly as in Group I. These cases, with the possible exception of Case 11, were considered to have a poor collateral blood supply to the lower limbs.

*Cecil John Adams Travelling Fellow, University of the Witwatersrand.

TABLE I.—*Results of Oral Priscol Therapy*

Case	Age	Diagnosis	Priscol mg.-day	Duration of Therapy	Arteriogram	% Decrease in Foot-minus-arm Time		Subjective Improvement		
						R	L	Loss of Pain and Paraesthesiae	Increased Warmth	Improvement in Claudication
					Group I					
1	61	Senile occlusive disease. B.P. 140/68	150	9 weeks	—	50	36	++	++	++
2	51	Multiple bilateral femoro-popliteal arterial emboli. B.P. 190/100. Mitral stenosis. Auricular fibrillation	300 150	10 ,,	—	14	15	+	+	Not present
3	49	Diffuse occlusive disease. Left femoro-popliteal thrombosis. B.P. 170/100	150	5 ,,	L. femoro-popliteal thrombosis. Irregular vessels	27	24	++	++	++
4	47	Diffuse occlusive disease	150	12 days	Bilateral femoro-popliteal thrombosis	58	40	Symptoms not present	+	++
5	75	Senile occlusive disease. Ischaemic neuritis. B.P. 240/100	150	5 weeks	—	No decrease		+	++	++
6	60	Senile occlusive disease. Right femoro-popliteal thrombosis. B.P. 154/90	150	4 ,,	Femoro-popliteal thrombosis (R)	,,	,,	+	+	+
					Group II					
7	60	Senile occlusive disease. B.P. 220/130. ? Old cardiac infarct	150	7 weeks	—	54	36	++	++	+
8	61	Senile occlusive disease. Gangrene right big toe. B.P. 155/95	150	12 ,,	Normal	53	56	++	++	+
9	66	Senile occlusive disease. ?Aortic saddle embolus. Myocardial infarction 1949. B.P. 126/89. Angina pectoris	150	6 ,,	—	44	44	++	++	++
10	64	Senile occlusive disease. Right femoro-popliteal thrombosis. Pre-gangrene. B.P. 190/90	150	8 ,,	—	30	17	+	+	Not known. Bedfast
11	65	Senile occlusive disease. B.P. 200/115. Pulmonary T.B.	150 300	1 week 4 weeks	L. deep femoral artery thrombosis	Nil	38	Nil	Nil	Nil
12	61	Senile occlusive disease. ? Aortic saddle embolus. Myocardial infarction 1943, 1949. Angina pectoris. B.P. 170/100	150	5 ,,	—	50	24	++	++	+

TABLE II.—*Results of Fluorescein Tests (Foot-minus-Arm Time (secs.))*

Case No.	Age	Diagnosis	Pre-treatment	During Treatment. After Reflex Heating	During Treatment. No Heating	Max. % Decrease During Treatment	Control
				Group I			
1	61	Senile occlusive disease. B.P. 140/68	R 10 L 11	5 7	5 7	50 36	9 9
2	51	Mitral stenosis with auricular fibrillation. Bilateral femoro-popliteal emboli. B.P. 190/100	R 14 L 15	12 13	10 11	29 27	— —
3	49	Diffuse occlusive disease. Left femoro-popliteal thrombosis. B.P. 170/100	R 15 L 17	11 13	11 14	27 24	11 17
4	47	Diffuse occlusive disease. Bilateral femoro-popliteal thrombosis. B.P. 140/90	R 14 L 10	6 6	— —	58 40	— —
5	75	Senile occlusive disease. Ischaemic neuritis. B.P. 240/100	R 9 L 6	7 19	7 17	22 0	13 11
6	60	Senile occlusive disease. Right femoro-popliteal thrombosis. B.P. 154/90	R 6 L 6	9 7	9 8	0 0	— —
				Group II			
7	60	Senile occlusive disease. B.P. 220/130. ? Old antero-lateral infarct	R 15 L 14	7 9	10 10	54 36	11 18
8	61	Senile occlusive disease. Gangrene right big toe. B.P. 155/95	R 17 L 18	10 8	8 10	53 56	12 15
9	66	Senile occlusive disease. ?Aortic saddle embolus. Myocardial infarction 1949. B.P. 126/89. Angina pectoris	R 16 L 16	9 9	10 10	44 44	8 8
10	64	Senile occlusive disease. Right femoro-popliteal thrombosis. Pre-gangrene. B.P. 190/90	R 17 L 12	14 10	12 10	30 17	— —
11	65	Senile occlusive disease. B.P. 200/115. Pulmonary T.B.	R 7 L 16	9 14	8 10	0 38	— —
12	61	Senile occlusive disease. ? Aortic saddle embolus. Myocardial infarction 1943, 1949. Angina pectoris. B.P. 170/100	R 18 L 17	12 13	9 16	50 24	8 16

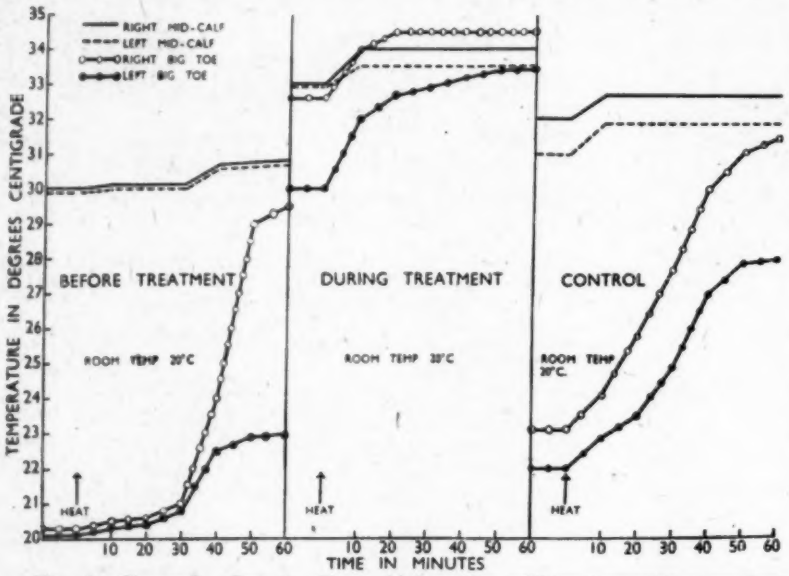

FIG. 1.—Group I. Case 1. Shows high resting calf–toe temperature gradient (10° C.) before treatment, reduction of gradient during treatment, and return of gradient to 9° C. after withdrawal of drug. Improved response of left great toe to reflex heating during treatment persists in some measure after withdrawal of priscol.

Prior to treatment the resting toe temperature before heating did not exceed 26.5° C. (Case 5), with the exception of Cases 3 (33° C.) and 11 (31° C.). In Case 1 the temperature was as low as 19° C. The small toe–calf gradient before heating in Cases 2, 3, and 11 may be explained by the presence of dilated collateral skin vessels (Pickering, 1933). The test was repeated after the patients had been taking priscol for seven to fourteen days, and in seven cases two to four weeks after the drug had been withdrawn.

Fluorescein Circulation Rate

The objective measurement of the circulation rate using skin fluorescence under ultra-violet light after the intravenous injection of fluorescein has been utilized by several workers (Lange and Boyd, 1942; Fishback *et al.*, 1942; Sicher, 1943; Winsor *et al.*, 1947).

We have used the technique of MacGregor and Wayne (1951), which one of us (J. F. G.), working in association with these authors, found entirely satisfactory.

With a solution of 1:1,000 histamine acid phosphate and 2% procaine, intradermal weals 0.5 to 0.75 mm. in diameter are raised on the left antecubital fossa, just below both knees, and on the dorsal surfaces of both feet. Then 4 ml. of a solution of 20% sodium fluorescein and 2% sodium bicarbonate is injected rapidly into a vein in the right antecubital fossa with the room in darkness. The interval between the first appearance of fluorescence in the weals and the beginning of the injection is measured with a stop-watch, the skin being illuminated by an ultra-violet lamp (Mercra 125 watt MBW/V, Range 3,130 Å–4,070 Å, 95% radiation concentrated at 3,650 Å). By this method a sharp end-point is obtained, the normal values being as follows:

	Arm-to-arm Time (Secs.)	Arm-to-Foot Time (Secs.)	Foot-minus-arm Time (Secs.)
Range:			
MacGregor and Wayne (1951)	9–25	21–35	8–13
Winsor *et al.* (1947)	15–25	25–35	9–11·2 (rarely 14)
Mean:			
MacGregor and Wayne (1951)	16·6	27·2	10·6
Winsor *et al.* (1947)	18·6	28·1	9·5

The foot-minus-arm time, which is obtained by subtracting the arm-to-arm time from the arm-to-foot time, measures the circulation rate in the lower extremities.

Times within the normal range are occasionally obtained in cases with definite organic disease, probably as a result of dilatation of collateral vessels. A difference in time between two legs is always abnormal.

A total of 46 fluorescein circulation estimations were carried out. All patients with occlusive disease were so investigated immediately after reflex heating, both before and during therapy. In 11 patients circulation rates were also estimated during treatment without previous reflex heating. Seven patients acted as their own controls, reflex heating and circulation rate estimations being carried out two to four weeks after withdrawal of priscol. No toxic effects were noted from the injection of fluorescein, except nausea in one case and vomiting in another. During treatment and investigation all patients, except Case 10 (early gangrene of toe), were ambulant, and were attending as out-patients in order to assess improvement under normal conditions. As the object of the investigation was to assess the long-term therapeutic value of priscol, tests were deliberately performed at random time intervals in relation to daily dosage. No other treatment was given, although patients were advised to avoid smoking.

Dosage and Duration of Treatment (Table I)

Initially 50 mg., thrice daily, was administered to all patients. In two patients (Cases 2 and 11) this was increased to 100 mg. thrice daily. The higher dosage was tolerated in Case 11 but not in Case 2. The duration of treatment varied from 12 days to 12 weeks, investigations usually being carried out one to two weeks after starting therapy.

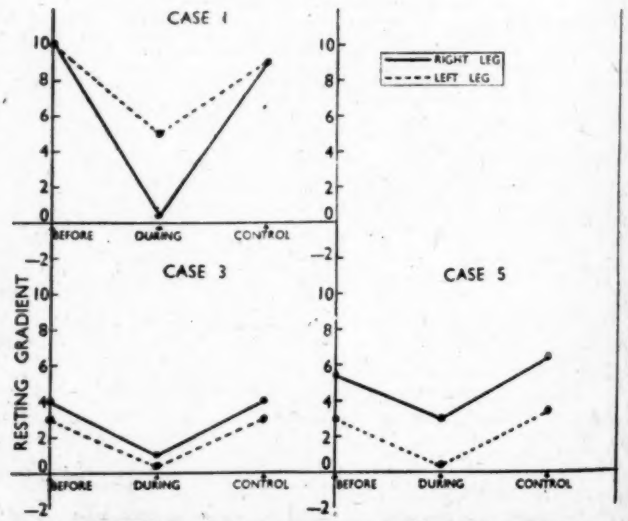

FIG. 2.—Resting calf–toe temperature gradient before treatment, during treatment, and two to four weeks after withdrawal of drug (control) in Group I. Shows abolition of gradient while on priscol, and return of gradient after withdrawal.

Toxic Effects

All patients noticed flushing of the whole body, mainly the lower extremity, headache, and "gooseflesh." These symptoms were seldom severe, and tended to wear off after two or three days' treatment. Case 6, a nervous patient with mitral stenosis and auricular fibrillation, found them disabling when on 300 mg. a day, but was able to take 150 mg. a day without ill effects. During treatment another patient (Case 12) developed epigastric pain and vomiting possibly due to stimulation of gastric secretion by the drug. The symptoms rapidly disappeared on withdrawal of priscol and on the administration of atropine. Subsequent priscol did not cause a recurrence of symptoms.

Results

Group I (Spastic Occlusive).—Fig. 1 shows the response to reflex heating before, during, and after termination of priscol therapy (control). Changes of this order were found in all cases in this group, both calf and toe temperatures being increased and the resting toe–calf temperature gradient being greatly reduced or even reversed while on treatment. In Cases 1, 3, and 5 (who acted as their own controls) the gradient was restored two to four weeks after stopping the drug (Fig. 2). Fig. 3 shows the effect of priscol on the toe–calf gradient in all cases in this group.

Group II (Occlusive).—Fig. 4 illustrates the responses to reflex heating in Case 12. The increase in temperature and the reduction in gradient are less marked, as is the response to priscol. In this group the results were much more variable, though the skin temperature of the toes was increased in every case while on priscol. Cases 7, 8, 9, and 12 acted as their own controls, and showed an increase in toe–calf gradient after

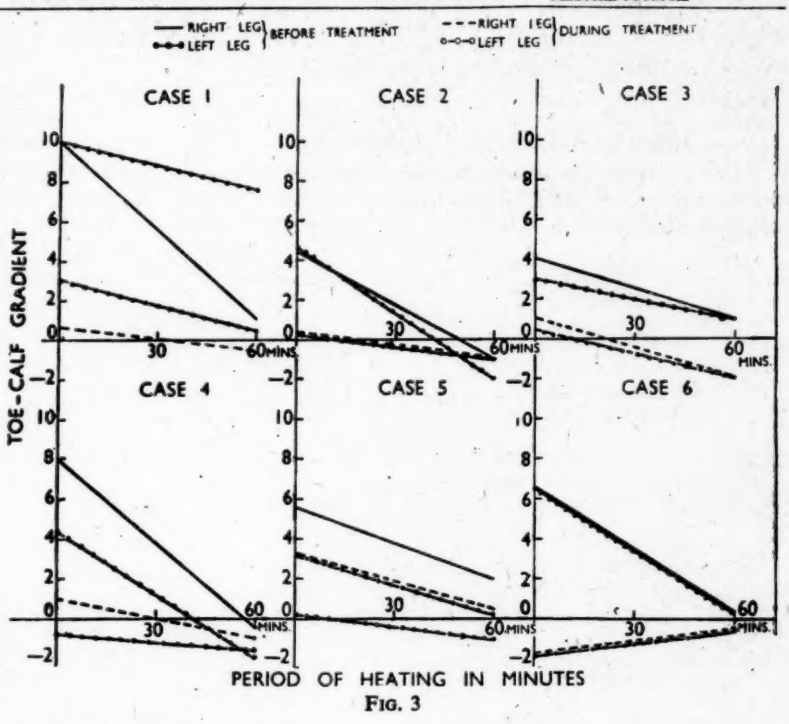

FIG. 3

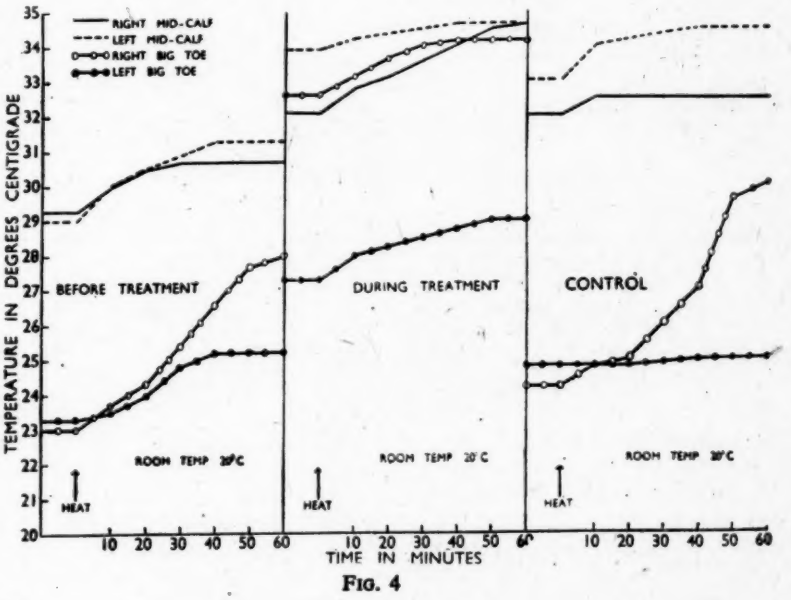

FIG. 4

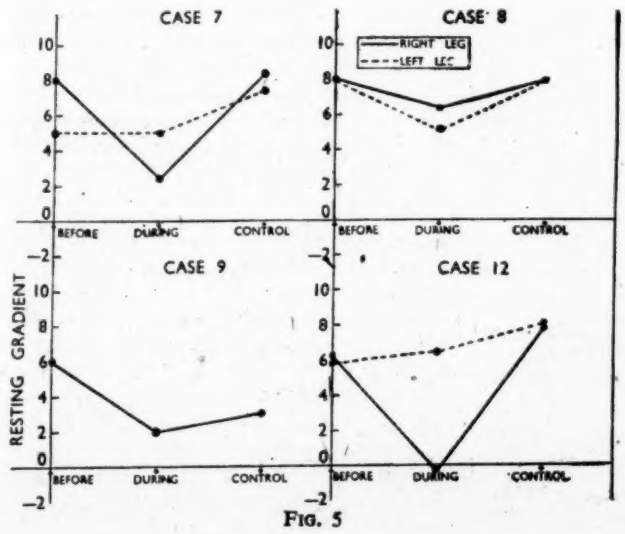

FIG. 5

FIG. 3.—Group I. Effect of priscol on the calf–toe temperature gradient change after reflex heating. Case 1 initially shows a gradient of 10 in right leg before heating, reduced to 1.5 after heating. During treatment, the gradient before heating is only 0.5 and after heating becomes reversed (−0.5)—that is, before treatment and without heating the right big toe is 10° cooler than right calf—after heating, temperature increases 8.5°. When on priscol the resting toe temperature is 9.5° higher and the gradient only 0.5. After heating, the toe becomes warmer than the calf, and the gradient is actually reversed. All cases in Group I show changes of same order.

FIG. 4.—Group II. Case 12. Shows elevation of toe temperature during treatment, and fall when treatment was stopped. Effect of priscol on calf–toe temperature gradient is very slight, though both calf and toe temperatures are elevated during therapy. Reflex heating does not alter the gradient appreciably, indicating absence of spasm and mainly occlusive changes in vessels.

FIG. 5.—Resting toe–calf temperature gradient before, during, and after treatment. Showing an increase in gradient after withdrawal of therapy.

withdrawal of therapy (Fig. 5). Fig. 6 shows the toe-calf gradients before and after priscol in Cases 7 to 12.

Effect on Fluorescein Circulation Rate

Table II shows the fluorescein times before treatment, during treatment (with and without previous reflex heating), and, in seven cases (1, 3, 5, 7, 8, 9, and 12), after the drug had been withdrawn. Maximum shortening of the foot-minus-arm time has been expressed as % decrease for each leg. In all cases except 5 (left leg), 6 (both legs), and 11 (right leg) an appreciable reduction occurred in the affected leg, varying from 17% to 56%, with an average of 38.7%. In 12 legs the foot-minus-arm time was reduced from an abnormal figure to one within the normal range. The average decrease was greater in Group II (43%) than in Group I (34.5%). These results are comparable with those obtained by MacGregor and Wayne (1951) in sympathectomized legs.

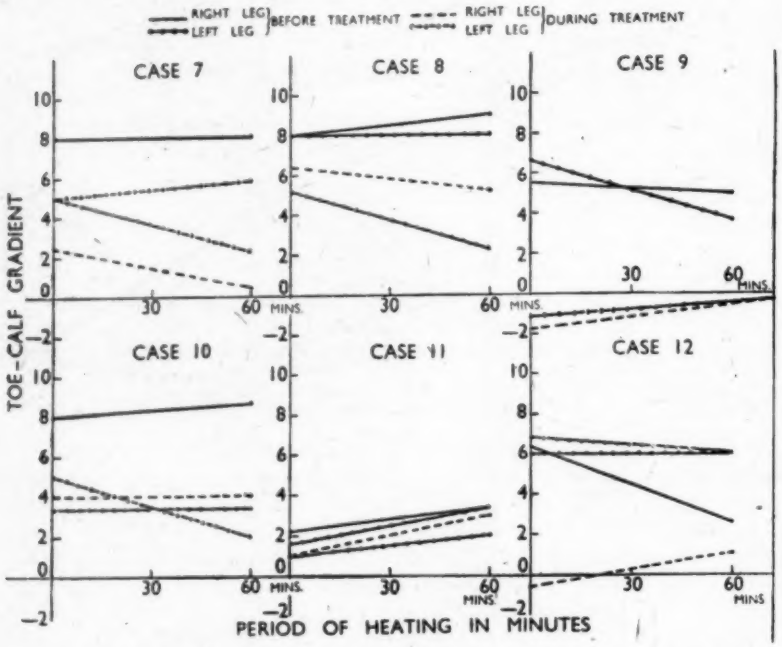

FIG. 6.—Shows that the effects of reflex heating and priscol on calf–toe temperature gradient are inconstant in patients with predominantly occlusive disease, but that there is a general tendency for the gradient to be reduced.

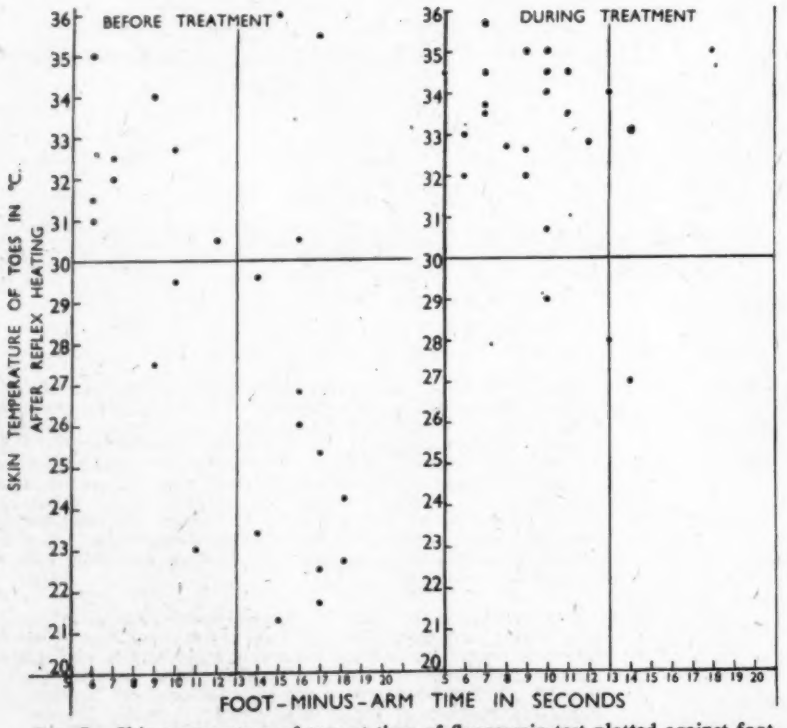

FIG. 7.—Skin temperature of toes at time of fluorescein test plotted against foot-minus-arm time before and during treatment. Each dot represents one leg. Apart from some scatter of points, the results before treatment show that the foot-minus-arm time tends to be short when toe temperature is high, and vice versa. During treatment most cases show high toe temperatures and short foot-minus-arm times.

Case 5 shows prolonged times in the left leg, and Case 6 in both legs, during treatment. The explanation of this is not clear, but in Case 5 at the time of the test the temperature of the left toe was high (35° C.), indicating dilatation of the arteriovenous anastomoses in the skin. It is possible that the local circulation was shunted through the anastomoses, by-passing the skin capillaries, and delaying the onset of fluorescence. Harpuder *et al.* (1940) have shown that the efficiency of the peripheral circulation in the presence of vascular disease depends upon the capillary circulation, and Popoff (1934) found that patent arteriovenous skin anastomoses may be present in patients with organic occlusive peripheral vascular disease.

Case 6 shows normal times throughout, possibly owing to the opening up of adequate collateral vessels, but abolition of calf–toe gradient and considerable symptomatic improvement occurred during treatment. Arteriography revealed occlusion of the right femoropopliteal artery (Table I). MacGregor and Wayne (1951) found that normal foot-minus-arm times could occasionally occur after reflex heating in patients with occlusive disease. Pickering (1933) also noted that normal skin temperatures were sometimes found in patients with organic disease. Case 9 showed no appreciable increase in gradient or lengthening of the foot-minus-arm time one month after withdrawal of priscol, indicating that a good collateral circulation was being maintained. Shortening of the right-foot-minus-arm time also persisted after withdrawal of the drug in Case 12.

Fig. 7 shows the relation of toe temperature to foot-minus-arm time in each limb, and it will be seen that, in the main, the length of the foot-minus-arm time varies inversely with the skin temperature, indicating that this circulation time is greatly influenced by skin blood flow. During treatment the majority of limbs show a high toe temperature and rapid foot-minus-arm times, suggesting that oral priscol increases the blood flow to the skin.

Subjective Changes During Treatment

All cases, except Case 11, experienced improvement in symptoms. Pain due to ischaemic neuritis, paraesthesiae, and numbness disappeared or was greatly reduced. The patients said that the legs felt warmer. No attempt was made to assess improvement in claudication accurately owing to the extreme difficulty in obtaining reliable results, even with graded exercise tests. Lynn (1950) found claudication to be unchanged by priscol, so that it was surprising to find that, out of ten of our patients who complained of claudication, nine said that they could walk further without pain and that the pain was less severe when it did occur. Case 11, however, who showed definite objective signs of improvement, persistently denied any subjective improvement whatever. He refused, however, to reduce his very large consumption of tobacco. Case 7 proved a disappointment. After obtaining great symptomatic and objective improvement for seven weeks, his condition suddenly deteriorated and he complained of a return of severe claudication in both legs, numbness, and rest pain. Although there was no great change in the physical signs, it was thought that further occlusion had occurred in the absence of adequate collateral vessels. In Case 9 amelioration of symptoms persisted even after priscol had been discontinued for one month.

The two patients suffering from Raynaud's disease showed normal reflex heating responses and normal fluorescein foot-minus-arm times after reflex heating before treatment, as was expected. The calf–toe and finger-to-arm temperature gradients were abolished and attacks did not occur during therapy.

Conclusions

The results obtained suggest that priscol is an effective vasodilator when administered orally to patients with occlusive arteritis. The most satisfactory results are seen in patients in whom vasodilatation of collateral vessels is possible. Definite, though limited, objective and subjective improvement can also occur in patients with advanced occlusive disease. In patients with mild degrees of disease priscol may be expected to afford considerable or even complete relief of symptoms, and may even delay the onset of more severe ischaemic changes. Priscol cannot be said to replace sympathectomy, but it may constitute a valuable alternative in patients unsuitable for or unwilling to undergo operation, and in early mild cases. In patients with acute occlusive ischaemic changes it may be of value as interim therapy while the extent of the disease and the suitability of the patient for operation are being assessed. It may well prove to be the treatment of choice in uncomplicated Raynaud's disease. Our results do not warrant any definite conclusion on the value of priscol in relieving the pain of intermittent claudication, but it must be remembered that even sympathectomy not infrequently fails to relieve this symptom.

The ease of administration and lack of serious toxic effects when given orally warrant its further trial in occlusive vascular disease. A long-term study of a large number of cases is necessary to assess fully the value of the drug.

Summary

Twelve patients with occlusive vascular disease and two patients with Raynaud's disease were treated with 2-benzyl-4,5-imidazoline hydrochloride (priscol) in a dosage of 75–300 mg. a day by mouth for periods of up to three months. Objective criteria of improvement were obtained in cases of occlusive disease, using the fluorescein circulation rate and reflex heating tests. Varying degrees of subjective improvement occurred in all except one case. Improvement in intermittent claudication was claimed by nine out of ten patients with this symptom. In the two cases with Raynaud's disease the attacks were completely prevented by priscol. Toxic effects were slight.

It is concluded that priscol is of some value in the treatment of ambulant cases of occlusive vascular disease, in patients unsuitable for sympathectomy, as an interim treatment in cases with acute ischaemia, and in patients with Raynaud's disease. Priscol is unlikely to replace sympathectomy, but further work is necessary to evaluate fully its place in the treatment of peripheral vascular disease.

We wish to thank Professor J. McMichael for his help and advice. The arteriograms were kindly carried out by Mr. Peter Martin and Mr. R. B. Lynn, of the department of vascular surgery.

ADDENDUM.—Since this paper was submitted for publication one of the patients with Raynaud's disease has suffered a return of the attacks with the onset of winter. These attacks are much less frequent and less severe than before starting treatment, and do not seriously inconvenience the patient.

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The Mecca pilgrimage, which annually draws thousands of pilgrims to the holy land of Hedjaz, in Saudi Arabia, will from now on be protected through a new set of health rules drafted by a special committee of the World Health Organization. These rules will become a part of the W.H.O. International Sanitary Regulations governing health aspects of all international travel by land, sea, and air, and have already been approved by a special committee. They were submitted to the fourth World Health Assembly, which opened in Geneva on May 7, and are intended to come into force in the middle of 1952. These special provisions will be inserted as addenda to the main regulations, and will replace the pilgrimage clauses of the 1926 International Sanitary Conventions established in Paris. The main modifications include for the first time provisions for the sanitary control of pilgrim aircraft. Two vaccinations only—against cholera and against smallpox—are obligatory for all pilgrims, whatever their country of origin or its sanitary condition, and if they come from a yellow-fever area they must be vaccinated against yellow fever. The quarantine station at Kamaran will no longer be used. This island in the Red Sea off Eritrea was an obligatory port of call for all pilgrim ships coming from the south on their way to Hedjaz. Adequate facilities will soon be provided at Jeddah, the main port of Saudi Arabia, which receives pilgrims from all parts of the world.

RESPONSE OF MEGALOBLASTIC ANAEMIA OF PREGNANCY TO CRYSTALLINE PENICILLIN G

BY

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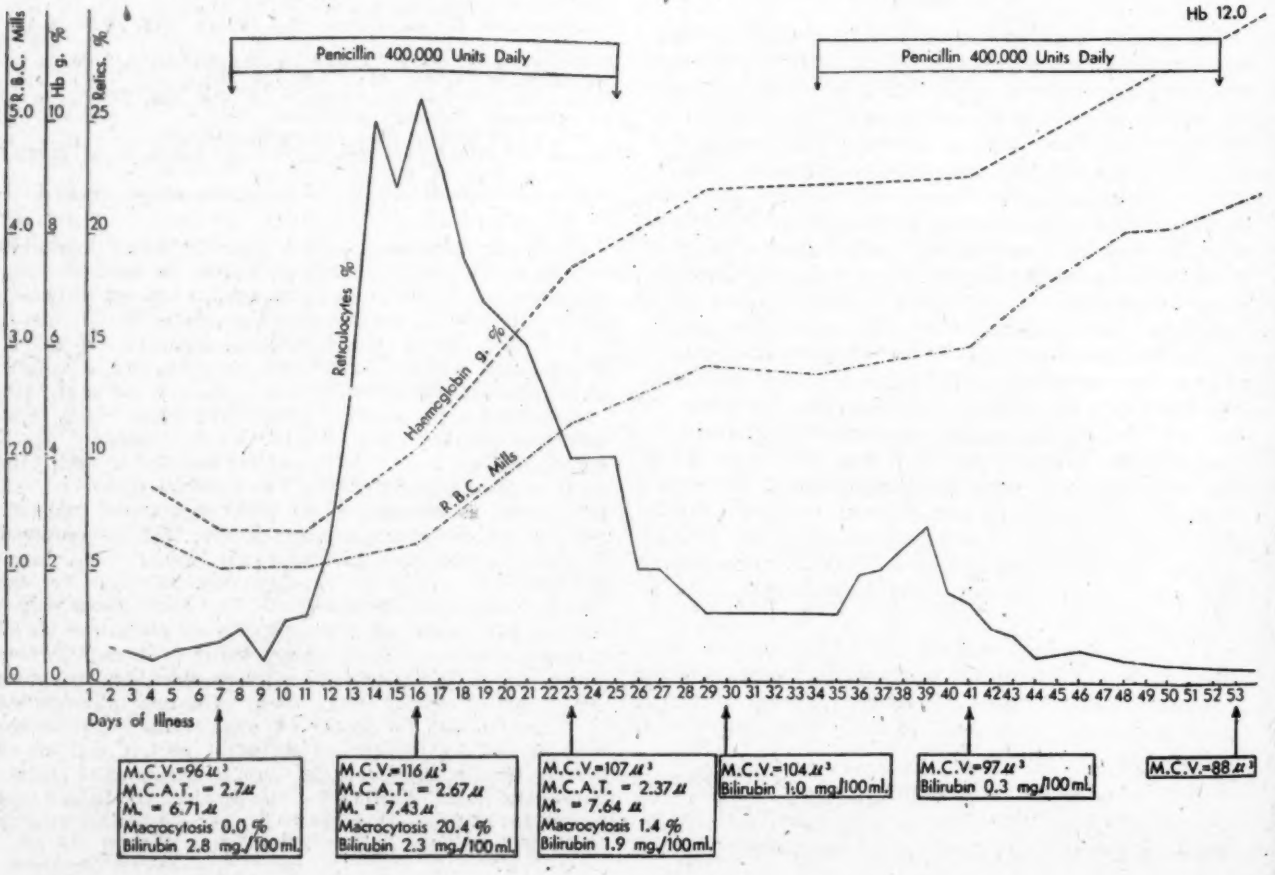
The purpose of this paper is to describe a case of megaloblastic anaemia of pregnancy which was successfully treated solely with injections of crystalline penicillin G, 400,000 units daily for 17 days. The reticulocyte, erythrocyte, and haemoglobin responses were maximal for the blood count and conformed to the criteria described by Ungley (1950) for 15th-day responses. The red-cell count and haemoglobin rose from 1,300,000 and 3.5 g.% to 4,300,000 and 12 g.%. The patient appeared to resemble the cases of megaloblastic anaemia of pregnancy which we saw in Macedonia (Fairley, Bromfield, Foy, and Kondi, 1938; Foy and Kondi, 1939) and those which Wills *et al.* (1930–4) have described from India. The women here are mostly apparently well nourished, and have a well-developed layer of subcutaneous fat and a high indirect van den Bergh reaction. It was previously suggested (Foy, Kondi, and Hargreaves, 1950) that their anaemias might be related to a deficiency of first-class protein.

In a previous paper (Foy *et al.*, 1951) we described the treatment of megaloblastic anaemia in a non-pregnant woman with a histamine-fast achlorhydria, who responded similarly to seven injections of penicillin G (2,800,000 units). This woman had had three previous relapses of anaemia, which had been successfully treated with either "marmite" or liver. Apart from the absence of nervous symptoms the case had appeared to be one of pernicious anaemia.

Case History

The patient, a negress six months pregnant, belonged to the Jaluo tribe inhabiting the eastern littoral of Lake Victoria. This is a hot, damp area with a heavy rainfall, much malaria, and considerable infestation with hookworm. The tribe itself has a sickling rate of 25%. The woman appeared to be well nourished and of good physique. She entered hospital on January 4, 1951, for weakness and breathlessness. We saw her first on January 6, when she was obviously gravely ill. Her liver was enlarged two fingerbreadths below the costal margin; her spleen was not enlarged; her nails, teeth, and tongue were all normal, as were her reflexes. Her heart and lungs showed nothing that was not compatible with her anaemic condition. She had one other child, aged 3, and she said that during that pregnancy she had been well, and had never had any anaemia. There was no history of miscarriages or abortions. Slight oedema of the ankles was present, and the upper lids were puffy. She said she ate meat three times a week—this may or may not have been so.

Reticulocyte counts were started on January 6, and a full blood examination carried out on the 11th is shown in the Chart. Price-Jones curves were done on January 10, when the reticulocytes were 1.6%, and, during treatment, on January 20, when they were 26%, and on January 27, when they were 10%. The M.C.A.T., mean diameter, macrocytosis, and M.C.V. for the various reticulocyte levels



are all given in the Chart. As will be seen, there is not always a good correlation between these variables, the lack of it being probably due in this case to spherocytosis (Foy and Kondi, 1943; Foy, Kondi, Hargreaves, and Lowry, 1950). A paper on the subject is now in course of preparation.

Before treatment the patient's marrow showed some intermediate megaloblasts and many giant stab-cells. Coombs's test was negative, and there was no sickling. A gastric test on February 5, after histamine, showed normal distribution of both free and combined acid. Schumm's test was positive, and the indirect van den Bergh was 2.8 mg. per 100 ml., indicating that there was some haemolytic process involved as in the Macedonian cases.

The Chart shows that the reticulocytes remained fairly stable at a low figure from January 6 to 12. On the 12th the patient received 200,000 units of crystalline penicillin G (sodium salt) twice daily, and similar amounts were given on the next 16 days. She said that she felt much better 24 hours after the first injection; this may have been merely a psychological reaction to an injection, but it is well known that similar feelings of well-being follow a liver injection. What was remarkable was the dramatic improvement in the patient's appetite.

On the seventh day of penicillin treatment her reticulocytes rose to 26%, and there was an improvement in the red-cell count and haemoglobin. On the sixteenth day after the beginning of treatment the red-cell count was 2,340,000, and the haemoglobin 7.4 g.%; on the twenty-second day the red-cell count was 2,830,000, and the haemoglobin 8.8 g.%.

As will be seen from the Chart, the penicillin was stopped on January 29 until February 7, and during this period the blood count remained unchanged or fell slightly, with the reticulocytes at about 3%. This stationary state occurred in our pregnant Macedonian cases with liver treatment, in which it was found that unless the liver was continued until the termination of pregnancy, or until the red-cell count had risen to between four and five millions, the patient either remained in a stationary condition or relapsed (Fairley *et al.*, 1938; Foy and Kondi, 1939). In the non-pregnant and in males it is necessary to continue the liver for only a few days after the attainment of the maximal reticulocyte response to ensure complete remission. In our previous case, that of a non-pregnant woman treated with penicillin, only seven days' administration was necessary to bring about a complete cure (Foy *et al.*, 1951). It seems that in pregnancy the extra drain on the haemopoietic system necessitates a continuation of treatment, or perhaps higher doses.

On February 7 the penicillin was again started in the same dosage. The reticulocytes rose to 7% on February 12, and on the 14th the red cells numbered 3,000,000 and the haemoglobin was 9 g.%. By February 17 the red cells numbered 3,500,000. At this stage the patient could be kept in hospital only with the greatest difficulty, and on February 26 she finally insisted on leaving. A complete blood examination done on this day showed that her blood count had risen to 4,300,000 and her haemoglobin to 12 g.%. The rest of the data appear in the Chart.

As a contrast to this case a non-pregnant negress entered the hospital with a megaloblastic anaemia, the red-cell count being 1,630,000 and the haemoglobin 4.2 g.%, and was given 80 μg. of vitamin B_{12} ("cytamen"). After two months her red-cell count was 3,470,000 and her haemoglobin 8.5 g.%. On February 19, three months after the last dose of vitamin B_{12}, the red cells numbered 3,600,000 and the haemoglobin was 10 g.%.

Discussion

This is the second case of dyshaemopoietic anaemia that we have treated with crystalline penicillin G. The response, as in the first case, was rapid, complete, and in every way similar to that obtained with liver, folic acid, and vitamin B_{12}. Crystalline penicillin (sodium salt) contains no vitamin B_{12} (Dr. Macrae, personal communication), and the mechanism by which the haemopoietic response is brought about cannot at present be stated with certainty. It is possible that the penicillin preparation contains some as yet unknown haemopoietic factor, or it may be acting as the so-called animal protein factor (when penicillin improves the growth of animals on certain diets). It is known that penicillin usually clears up cases of infantile diarrhoea, and penicillin, streptomycin, and chloramphenicol are all known to affect the flora of the gut both qualitatively and quantitatively, penicillin being the least radical in its effect. "Aureomycin" is stated to clear the gut almost completely of its flora, and unless vitamins are given with it vitamin deficiency may result. Whether all these antibiotics are affecting the same organism in the gut is unknown; it is likely, however, that some of them deal with one organism and some with another.

Rominger (1950) has claimed that in infants treated with streptomycin there is no change in the intestinal flora, and that the effects of this drug are in his opinion due to the elimination of toxins the origin of which are unknown. From work on baboons with megaloblastic anaemia we believe that the elimination of "toxins" produced by intestinal organisms may be an important factor in the results that we have been obtaining.

Cameron and his colleagues (1949) have suggested that in the megaloblastic anaemia occurring with intestinal stricture there may be a change in the flora of the gut that leads to the loss of an organism that synthesizes haemopoietic factors, or to the production of an organism that competes for haemopoietic factors, or to the production of antagonists. Aureomycin has been found to prevent the development of this kind of anaemia.

It has generally been assumed that the lack of first-class protein, or some factor contained therein, is important in the genesis of the megaloblastic anaemias of pregnancy and the so-called nutritional megaloblastic anaemias. We wonder, however, whether deficiency of protein is as important as other items in the diet, such as high intake of bulky carbohydrates, as has been found to be the case with rats. A deficiency of the first and an overabundance of the latter may produce an intestinal environment that is unsuitable for the synthesis and absorption of haemopoietic substances, or affect the liver. In most countries where we have worked, and where these megaloblastic anaemias are prevalent, the diet of large sections of the peasants consists predominantly of bulky carbohydrates (Greece, South Africa, Bechuanaland, Mozambique, East Africa). The line of demarcation between these megaloblastic anaemias of pregnancy, those of nutritional origin and pernicious, seems to become less and less clearly defined as knowledge progresses, and the terms "extrinsic" and "intrinsic" factors would seem to us to need revision.

It is not impossible that the relapses and remissions that occur in pernicious anaemia may be associated with changes in the intestinal flora, leading to the destruction or formation of haemopoietic substances such as vitamin B_{12} or folic acid (Hunter, 1909; Noer, 1950). If bacterial synthesis is an important source of haemopoietic factors, then it might be possible by means of aureomycin to produce relapses, as it is known that both aureomycin and terramycin "antagonize" penicillin (Gunnison *et al.*, 1950).

Penicillin may bring about its effects by preventing bacteria utilizing essential substances that the body needs for synthesis of haemopoietic substances or nucleo-proteins; it may do this by modifying the flora of the gut (Krampitz and Werkman, 1947) or by interfering with the absorption of glutamic acid or other substances by bacteria in the gut (Gale and Taylor, 1946).

Work is continuing on further cases and by the use of additional methods; we therefore propose to defer further discussion until we can deal with the matter more extensively.

Summary

After the successful treatment of histamine-fast achlorhydric megaloblastic anaemia with crystalline penicillin G (sodium), this substance has been used without other treatment in the megaloblastic anaemia of pregnancy with the same striking results.

A maximum reticulocyte response was observed within five to eight days after the first injection. On the fifteenth day the expected red-cell count and haemoglobin level were reached. The patient was discharged with a red-cell count of 4,300,000 and a haemoglobin level of 12 g.%.

In both these types of megaloblastic anaemia the response to penicillin was similar to that which we have obtained with crude or refined liver, vitamin B_{12}, or folic acid. The marrow reverts to the normal picture, the megaloblasts disappearing rapidly and the giant stab-cells more slowly.

It is suggested that this response to penicillin may be due to any or all of the following: (1) changes in the flora of the gut, which may lead to the destruction of antagonists or competitors, or other factors which may be interfering with the synthesis, absorption, or utilization of haemopoietic factors; (2) interference with bacterial metabolism, thus releasing haemopoietic factors for the use of the body; (3) an effect on protein metabolism and the synthesis of nucleo-proteins from basic amino-acids; (4) the presence of hitherto unknown haemopoietic factors; and (5) the destruction of toxins produced by bacteria.

Our thanks are due to the Director of Medical Services, Kenya, for permission to publish this study; to the Medical Research Laboratory for innumerable facilities; and to the medical and nursing staff of the King George VI Hospital, Nairobi, for its unfailing assistance throughout.

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A survey has been conducted for the Ministry of Health on the use of hearing-aids. A small proportion only of patients use their aids for the maximum period of 15 hours a day, and about half do not use them for more than five hours. Only one in five uses his aid for more than 10 hours a day. Several ways of economizing in battery consumption have been suggested as a result.

THE CLINICAL SIGNIFICANCE OF VITAMIN-A DEFICIENCY*

BY

Z. A. LEITNER, M.D.

During recent years my colleagues and I have been working on different aspects of vitamin-A deficiency in man. I propose to outline here briefly some of our results, together with a critical review of the literature.

General Considerations

The sequels of vitamin-A deficiency have been studied extensively on experimental animals during the past 25 years. Most impressive changes were observed in the epithelial tissues: atrophy of the epithelial layer followed by reparative proliferation of the basal cells, with growth and differentiation into a stratified keratinizing epithelium (Wolbach and Howe, 1925). These changes occur presumably in all vertebrates, including the foetal stage (Wilson and Warkany, 1947). Epithelial cells with secretory function are predominantly affected (salivary glands, respiratory tract, eyes, skin, genito-urinary tract); keratinization in the secretory cells may produce severe obstruction with cystic dilatation of the gland ducts and accumulation of debris leading to secondary infection (Wolbach and Bessey, 1942). On the other hand, epithelial cells with chemical function—for example, liver cells—do not exhibit marked atrophy or keratinizing metaplasia. Further important tissue changes were observed in the skeleton.

In rats vitamin-A deficiency established at an early stage retarded the enchondral and stimulated the periosteal bone formation. In puppies and rabbits reared on a vitamin-A-deficient diet bony overgrowth of the labyrinth and thickening of the cranial bones (Mellanby, 1938, 1941) was observed, whilst the soft tissues continued to grow normally. Owing to this disproportion between growth of bone and nerve tissues an overcrowding of the cranial cavity, with multiple herniation of the cerebrum and cerebellum into the dural sinuses and compression of the cranial nerves, occurred. For the same reasons spinal-nerve roots herniated into the intervertebral foramina, and thus the mechanical pressure led to degeneration of various cerebral tracts and peripheral nerves (Mellanby, 1939, 1943). However, some degenerating influence of vitamin-A deficiency on the nerve tissue seems to persist (Irving and Richards, 1940).

The normal human organism has the tendency to maintain a more or less constant individually characteristic blood vitamin-A level which is only temporarily affected by the transitory fluctuations of vitamin-A intake. Under the same nutritional conditions healthy male adults seem on the average to have 10–20% higher vitamin-A values than females. Children up to the age of 16–17 have somewhat lower values than adults. The vitamin-A levels in pregnant women are lower than in non-pregnant women; the diminution is most pronounced during the last trimester of pregnancy. Within 24–48 hours after delivery, without any change

*Based on an address to the Nutrition Society. (Vitamin A Conference, Liverpool, September 23, 1950.)

of the diet, a sudden rise occurs. The vitamin-A level of the newborn is about half that of the normal adult, and it is independent of the maternal plasma vitamin-A level. Three or four days after birth the vitamin-A level suddenly increases. The regulating mechanism for these processes seems to be linked with the intact liver, which stores more than 90% of all vitamin-A reserves of the body.

Congenital Abnormalities related to Vitamin-A Deficiency

Animal experiments furnish sufficient evidence that a nutritional deficiency during pregnancy does not necessarily lead to deficiency signs in the mother. The offspring may, however, in consequence die during the first few days of life. Another observation which seems to be of great significance is that the occurrence of a congenital malformation may be enhanced by deficiencies in the antenatal diet. It appears that a latent tendency to a congenital trait which may only rarely become manifest under adequate nutritional conditions may become more frequently overt if the diet during pregnancy lacks certain nutrients. Whilst the application of these conclusions to man is difficult, it can be reasonably assumed that neonatal mortality and the incidence of congenital malformations in humans increase under unfavourable nutritional circumstances.

The effect of different degrees of malnutrition during gestation in experimental animals may be summarized as follows: general starvation before conception results in sterility; if starvation starts in early pregnancy the embryo dies; starvation in the later stages of pregnancy may result in stillborn or underweight offspring. If the maternal calorie intake is sufficient, but certain essential nutrients—for example, vitamin A—are not available at the time of the organogenic period, a borderline deficiency is created at that critical time and congenital malformations may easily occur. The addition of only minimal amounts of the specific nutrient may result in normal offspring; further slight restriction of these nutrients, on the other hand, may lead to embryonic death (Warkany, 1947). These facts emphasize the importance of environmental factors in the production of congenital abnormalities. Since the discovery of prenatal rubella as a teratogenic factor capable of inducing congenital malformations in man, for which genetic factors are not responsible, deficiency of specific nutrients during pregnancy has acquired increased significance (Leitner, 1950, 1951).

Experiments on Rats

In carefully conducted experiments on rats on a vitamin-A-deficient diet about 75% of the offspring showed multiple ocular changes (Warkany and Schraffenberger, 1946), such as fibrous retrolenticular membrane in place of the vitreous body, colobomas, eversion of the retina, and rudimentary development of the iris, of the ocular chambers, of the ciliary body, and of the cornea; in addition abnormalities of the genito-urinary tract were often present (Wilson and Warkany, 1948). In about 44% of the same series congenital cardiac deformities were found, including septal defects, abnormalities of the aortic arch and pulmonary vessels, patent ductus arteriosus, and retardation of myocardial development (Wilson and Warkany, 1950). None of the abnormalities were seen in the controls.

Many of the cardiac and eye abnormalities in rats closely simulated malformations encountered in man. It would, however, be absolutely unjustified to apply without reservation the results of such experiments to human beings or to suggest that maternal dietary deficiency was an important cause of congenital malformations in man (Leitner, 1950, 1951). These experiments should only widen our understanding of teratogenic factors by demonstrating that a maternal metabolic imbalance (in this case a vitamin-A deficiency) may interrupt the normal nutrition of the embryo during the organogenic period and thus conceivably lead to abnormal development. It shows also that development of organs may be similarly altered by either genetic or environmental factors (Warkany, 1947).

Pityriasis Rubra Pilaris

In man there are two rare inherited diseases which have, as it is claimed, some relationship to vitamin-A deficiency. I referred to the ambiguous topic of the fibrocystic disease of the pancreas elsewhere (Leitner, 1951), but I should like here briefly to mention pityriasis rubra pilaris. After having collected 152 cases from the literature, I was able to demonstrate with the help of Ford that pityriasis rubra pilaris is always inherited, probably as a simple autosomal heterozygous condition without sex control and without linkage with the ABO blood-group series. The apparently non-familial cases are due only to mutation (Leitner and Ford, 1947; Cockayne, personal communication, 1950).

I have encountered two patients with pityriasis rubra pilaris in whom, in spite of thorough search, no other affected members of the family could be traced. One of these, a man in whom the disease was first noticed at the age of 63, had normal ancestry and children; his daughter, however, a well-nourished healthy woman without any sign of skin disease, had a pathologically low vitamin-A level (Barber and Leitner, 1951). Such skipping of a generation or reduced expressivity of a gene has been repeatedly observed in families with heterozygous or recessive abnormal traits; lesser degrees of abnormalities—for example, low vitamin-A level—or slight deviations from the normal may more often be detected, but only by special examinations. The second patient suffered from syringomyelia in addition to pityriasis rubra pilaris (Barber and Tatz, 1946). In this case two different systems of ectodermal origin—skin and central nervous system—were involved in the same patient (Leitner, 1946a).

Clinical Conditions related to Vitamin-A Deficiency

The vast literature on the manifold symptoms and signs of vitamin-A deficiency appears to be disproportionate to the predominantly negative results of the Sheffield experiment (Medical Research Council, 1949). One reason for this may be that in clinical medicine, in contrast to the healthy young conscientious objectors of Sheffield, we deal with subjects of every age group with known and unknown impairment of the organs. In addition, patients are usually exposed to a number of conditioning factors (Leitner, 1948b). Moreover, signs and symptoms due to lack of water-soluble vitamins are more acute and more easily detectable than those related to deficiency of vitamin A, of which reserves may be stored for one to two years. For these reasons any discussion of the clinical aspect of vitamin-A deficiency should not be considered as a statement of facts but rather as an assessment of views at present prevalent.

Vitamin-A Deficiency and Involvement of the Eye

Hemeralopia.—The retina contains two types of photoreceptor cells—the cones active in daylight and in colour (photopic vision), and the rods functioning in dim light and darkness (scotopic vision). When light falls on the rods certain chemical changes occur in the visual purple (rhodopsin), which in some form is always present in the walls of the rods. Rhodopsin, in which the prosthetic group appears to derive from vitamin A, is bleached by bright light and regenerated in the dark within a few minutes (dark adaptation). Since vitamin A is necessary for this process, hemeralopia might be one of the earliest signs of vitamin-A deficiency. (Other causes of hemeralopia are outside the scope of this paper.)

Bitot's Spots.—These consist of a slight, usually triangular thickening of the scleral conjunctivae with accumulation of white foam-like epithelial cells situated laterally from the cornea, with the base directed towards the limbus. Concomitant signs of the underlying malnutrition are often hemeralopia or phrynoderma. Bitot's spots are rare in temperate climates, and have to be differentiated from the more frequent pingueculae which are not of epithelial origin or related to malnutrition.

Xerophthalmia.—Xerosis of the conjunctiva may be a sequel of local disease (trachoma, pemphigus, injuries) or of malnutrition. In the early stage, which can be fairly often observed, there is a loss of lustre and rapid desiccation. The latter is especially noticeable if the eyelids are kept open for over half a minute, and is due to atrophy of the epithelial cells, followed by hyperkeratosis and involvement of the lacrimal glands, leading to a further drying up of the secretion. In the later stages irregular patchy, occasionally confluent subepithelial opacities may be observed (Williamson-Noble, 1942).

Keratomalacia.—As the xerosis advances the cornea becomes dull, softened, and infiltrated, followed by ulceration, hypopyon, abscess formation, and perforation.

While hemeralopia and early xerosis are not infrequently met with, the other conditions are very rare in this country.

Vitamin-A Deficiency and Skin Diseases

As mentioned earlier, keratinizing metaplasia of the epithelia may be regarded as the characteristic change in vitamin-A deficiency. There is little doubt about the indispensability of vitamin A for the normal metabolism of epithelial surfaces. In spite of this the presence of vitamin A could not be detected even after feeding excessive amounts of vitamin A either in the epidermis (Cornbleet and Popper, 1942) or in the epithelium of mucous membranes, which are considered the first sites of vitamin-A deficiency (Popper, 1941). A varying degree of hyperkeratosis, comparable to that seen in man—the extent of which was inversely related to the amount of ingested vitamin A—was caused in rats (Moult, 1943). But no unequivocal follicular keratotic changes could as yet be produced experimentally in man, although the vitamin-A deprivation was maintained at times for as long as 25 months (Medical Research Council, 1949).

The extensive literature on human skin diseases attributed to vitamin-A deficiency has been reviewed in previous papers (Leitner 1945, 1948a; Leitner and Moore, 1946; Leitner and Ford, 1947). We have no knowledge about the mechanism of vitamin-A utilization, either regarding its transfer to the epithelial surfaces or its interrelationship with other factors, such as vitamin-C deprivation (which may also cause follicular hyperkeratosis), the B vitamins, or trauma (Stannus, 1945). Moreover, vitamin A is usually administered in oily solutions containing the "essential" fatty acids ("vitamin F"), which are also claimed to be necessary for the maintenance of the normal skin (Hansen, 1937).

In treating deficiency states 10 to 20 times the minimum daily requirement is considered to be an adequate therapeutic dose. The fact that in most follicular keratotic conditions well over a hundred times the minimum daily requirement is needed indicates that vitamin-A deficiency itself cannot be the only cause of these changes. The therapeutic effect thus conferred may not necessarily be specifically nutritional; it might perhaps be "pharmacological" (for example, influencing an allergic state or a hypochlorhydria); it may also act by "supercharging"—that is, the surplus of vitamin A may exceed the storing capacity of the liver and it may therefore appear in tissues from which it was excluded by the disease, and thus restore an equilibrium which in turn controls the regeneration of epithelial tissues.

Many skin conditions have been associated with vitamin-A deficiency—for example, phrynoderma (Nicholls, 1933), ichthyosis (Rapaport *et al.*, 1942), acne vulgaris (Straumfjord, 1943), leucoplakia vulvae (Hyams and Bloom, 1947), pili torti (Siskind, 1947)—and therapeutic successes have been reported. Some of our own experiences with Darier's disease and pityriasis rubra pilaris might be of interest (Leitner, 1946b; Leitner and Moore, 1946, 1948; Leitner and Ford, 1947). Both conditions are characterized by diffuse hyperkeratosis in relation to the pilosebaceous glands and hair follicles, with intrafollicular horny plugs projecting above the surface, localized to certain parts, or scattered all over the whole body.

Table I shows the mean plasma carotenoid and vitamin-A values in 105 hospital patients suffering from a variety of common skin diseases, and those of 116 healthy subjects and hospital patients suffering from conditions which most likely do not alter the vitamin-A level. The figures are almost identical. Table II

TABLE I.—*Plasma Carotenoids and Vitamin A in Cases of Common Skin Disease and in Controls*

	Mean Values (i.u. per 100 ml.)	
	Carotene	Vitamin A
Skin disease group (105 cases) ..	130	120
Control group (116 cases)	139	113

TABLE II.—*Plasma Carotenoids and Vitamin A in Patients with Darier's Disease and Pityriasis Rubra Pilaris*

Disease	No. of Cases	Before Dosing				After Dosing
		Mean Values		Lowest Values		Max. Vit. A
		Carts	Vit. A	Carts	Vit. A	
Darier's disease ..	9	116	79	94	55	837
Pityriasis rubra pilaris	8	109	86	86	61	344

shows the abnormally low values in nine cases of Darier's disease and eight cases of pityriasis rubra pilaris. In agreement, however, with other workers (Peck *et al.*, 1943; Carleton and Steven, 1943; Porter *et al.*, 1947), we occasionally found normal vitamin-A levels in both conditions. With a few exceptions the initial vitamin-A level corresponded roughly to the clinical involvement. In our cases of Darier's disease it was lower than in the patients with pityriasis rubra pilaris; on the other hand, the rise in the vitamin-A levels after dosing was much higher, and was attained in a shorter time in Darier's disease. The condition of most of our patients improved under vitamin-A treatment, often considerably, but complete clinical cure was exceptional. There was no direct relation between high vitamin-A level after dosing and improvement—for example, in a case of Darier's disease the vitamin-A level was maintained between 800 and 1,800 i.u. for over three years, but the improvement of the skin condition was minimal. Yet a patient with a severe exfoliative type of pityriasis rubra pilaris who never reached vitamin-A values above 227 i.u. was healed clinically after four months' treatment (Barber and Leitner, 1951).

Vitamin-A Deficiency and Diseases of the Liver

The occurrence of dry, rough skin with or without xerophthalmia and keratomalacia in jaundiced children was repeatedly described towards the end of the last century. Moore (1929) was the first to demonstrate that rats fed on carotene stored vitamin A in the liver; and later he showed that about 95% of the vitamin-A reserve is stored in the liver (Moore, 1931). Since then attention has been focused more and more on the disturbance of vitamin-A metabolism in hepatic diseases.

In liver diseases not only the absorption of vitamin-A seems to be impaired (Breese and McCoord, 1940) but also its release from the liver (Popper *et al.*, 1943). In liver cirrhosis both the vitamin-A reserves in the liver (Moore, 1937) and the plasma vitamin-A level are reduced (Haig and Patek, 1942). Vitamin-A tolerance curves seem to indicate that the blood vitamin-A level in man is related to the extent of the actual liver damage (Popper *et al.*, 1943). Thus in infective hepatitis a plasma vitamin-A level below normal was found, though the liver stores were proved to be adequate (Harris and Moore, 1947). The change in plasma vitamin A is considered by some authors "a valuable and sensitive indicator of hepatic function," and it is suggested that it may develop into a test for liver damage (Aron, 1949). The selection of special liver-function tests is indeed of the greatest importance (Gray, 1950). This may explain that, whilst we found (Leitner and Moore, 1946, 1948) severe impairment of the liver function in some cases of Darier's disease and of pityriasis rubra pilaris, Porter and Brunauer (1949), using different liver-function tests, could find only minor abnormalities.

The urinary excretion of vitamin A often occurring in diseases of the kidney and of the genito-urinary tract (Moore, 1951) may also be related to the inability of the damaged liver to store the vitamin.

Vitamin-A Deficiency in Febrile Conditions

Extremely low plasma vitamin-A levels were reported repeatedly in pneumonia and other feverish diseases. But surprisingly high liver stores were found at necropsy in some children whose plasma vitamin-A values were extremely low and hardly measurable a few days before death (Lindqvist, 1938). In convalescence after febrile diseases much higher vitamin-A levels were sometimes found than before the onset of disease.

In 92 patients suffering from venereal diseases physically induced hyperthermia was given in combination with chemotherapy, and the elevation of body temperature up to 105.5–106° F. (40.85–41.1° C.) was followed by depression of plasma vitamin A and carotenoids (Aron *et al.*, 1946). The diminution both of the carotenoids and of the vitamin-A levels was directly related to the duration of fever—about 10% after three hours, 20% after six hours, and 30% after eight hours of fever. A definite rise was observed on the second morning after termination of the fever treatment, and on the third morning the plasma vitamin A returned to the original level without any medication or dietary supplements. On the other hand, a considerable and persistent fall of the vitamin-A level was recorded in acute rheumatism, the degree of which varied directly with the intensity of the rheumatic attack, but it was not related to the degree of pyrexia (Shank *et al.*, 1944).

Since 1944, in collaboration with Drs. A. L. Jacobs, T. Moore, and I. M. Sharman, I have been engaged (Leitner *et al.*, 1947; Jacobs *et al.*, 1951) in investigating whether the infectious process as such or the pyrexia was responsible for the depression of the plasma vitamin-A level. The evaluation of these results has not yet been concluded, but I may perhaps be allowed to give here my personal impressions at the present juncture. Our material consisted of over 300 hospital in-patients, including over 100 suffering from rheumatic fever, about another 100 with various pyrexial diseases (pneumonia, pleurisy, tonsillitis, etc.), and about 100 more with miscellaneous illnesses. The patients were equally divided in sex. The age of the rheumatic group ranged from 5 to 60, with an average of 20.5 years and with 64% between 5 and 19 years. The other groups included more middle-aged subjects. The plasma vitamin-A level in our material declined with increasing body temperature to about the same extent in rheumatic fever, pneumonia, pleurisy, tonsillitis, and erythema nodosum. This inverse relation between body temperature and vitamin-A level was, however, not constant, and is being evaluated statistically at present.

A sudden and considerable increase of circulating plasma volume was reported recently in rheumatic fever (Reid *et al.*, 1950). Bradley (1951) attributed the sudden anaemia and unexpected heart failure to this haemodilution. A correlation of our results with the very few blood-volume estimations in rheumatic fever so far published is not yet possible. It appears also that the fall of the vitamin-A level in our patients was not in proportion to the blood dilution and it seemed to be greater than in experimentally produced fever. In the present state of our knowledge I am inclined to attribute this depression simply to disturbances in the vitamin-A metabolism. At the outset the deviation might seem to differ very little in the various pyrexial states. In rheumatic fever, however, some other factors have to be considered in addition, such as a prolonged course of the disease and repeated relapses, often at an age when the normal requirements for growth and development are increased. This line of

thought seems to be corroborated by the results of a pilot experiment carried out in collaboration with Dr. C. E. Thornton some years ago. We had the impression that a daily supplement of 40,000–50,000 i.u. of vitamin A given to rheumatic children during the phase of relapse was beneficial (Thornton, 1946).

Only scanty information exists regarding the effect of fever on the vitamin-A level in pregnancy. Bicknell (1950) suggested that in those cases of pregnant women suffering from German measles in which the termination of pregnancy was not considered vitamin A should be given. I extended this suggestion, proposing that vitamin A should be administered in every case of pregnancy complicated by infection or fever, especially during the first trimester, which approximately corresponds to the organogenic period (Leitner, 1950, 1951).

Conclusion

The work briefly reported here demonstrates the importance of an adequate plasma vitamin-A level during the embryonal development and in some clinical conditions such as ocular, dermatological, hepatic, and febrile diseases.

I should like to conclude this report with two suggestions which seem to be justified by the present state of vitamin-A research, though their strict therapeutic necessity cannot yet be substantiated. I would advocate supplementing the routine treatment in the acute stage of rheumatic fever with 40,000–50,000 i.u. of vitamin A daily. The same dose of vitamin A should be administered in pregnancy complicated by infection or fever, especially during the first trimester. No special claims are attached to these, as yet tentative, suggestions, and it is hoped that further research will support and possibly amplify them.

It is a great pleasure to acknowledge the collaboration or the generous help given by so many colleagues during the long course of these investigations. My grateful thanks are due particularly to Sir Allen Daley, Drs. H. W. Barber, F. J. Bentley, E. B. Ford, L. J. Harris, A. L. Jacobs, I. M. Sharman, G. B. Mitchell Heggs, and C. E. Thornton. I am especially indebted to Dr. T. Moore for his valuable help, friendly advice, constructive criticism, and continuous encouragement.

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THE DISTRIBUTION OF ANOPHELINE MOSQUITO BITES AMONG DIFFERENT AGE GROUPS

A NEW FACTOR IN MALARIA EPIDEMIOLOGY

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While it has been known for a long time in a general sort of way that some individuals are more attractive to mosquitoes than others, little attempt has been made to follow up the wider implications of this and see whether any particular age group is more attractive than others. Nothing whatever was known about whether children were bitten more by anopheline mosquitoes than adults, or whether, say, babies were more attractive than their mothers. There was really nothing to give us any idea of what happens when an anopheline mosquito enters a native house and is faced with a choice of biting babies, children, or adults. In the absence of such information it has been necessary in discussing problems of malaria transmission and epidemiology to assume a random distribution of bites among an equally accessible human population, an assumption which, however, has given rise to many inconsistencies.

For some time now I have been concerned with this serious gap in our knowledge, without, however, being able to overcome the technical difficulties. In many tropical countries, particularly in Asia and Africa, the

anopheline vectors of malaria bite mainly indoors at inconvenient hours of the night. Biting is often so intermittent that prolonged observation inside native village houses would be necessary to give conclusive results. In these circumstances there are obvious limits to the amount of co-operation one might expect from the householders and their families. The indirect approach has been considered in which members of the family might be treated with different drugs in such a way that the minute quantity of blood extracted by the mosquito would show the presence or absence of the drug among engorged mosquitoes found in that house, thus indicating which members of the family had provided the blood meal. Although attempts on these lines have met with no success, there is a distinct possibility that a satisfactory technique will be worked out in time.

In contrast to the anophelines of the Old World, the habits of *Anopheles albimanus*, a widespread vector in Central America and the Greater Antilles, lend themselves particularly well to the investigation of this problem by direct observation. In Jamaica, *A. albimanus* bites man actively outdoors as well as indoors. There is a sharp peak of biting at sundown, when most village people are sitting or moving about out of doors: and there is another sharp peak of biting at dawn, when many people, particularly the children, are still asleep in bed. During these peaks the numbers of *A. albimanus* attempting to bite are often large enough to give significant figures in quite a short time.

Present Investigation

A few random observations on mothers and their babies soon revealed a striking difference in that for each bite or attempted bite on the baby about 20–30 mosquitoes could be taken attacking the mother, most babies remaining completely free of bites during this peak at dusk. In this mosquito-infested area the co-operation of a Jamaican negro family was obtained, and routine observations were made on the whole family seated out of doors at sundown. The observations extended over several months and covered a wide range of climatic conditions and mosquito abundance. Mosquitoes settling on each person and attempting to bite were picked off by means of a sucking tube and recorded as "bites." Whether these bites would normally be followed by blood feeds is quite a different matter; this is discussed later. The youngest members of the family were soon trained to sit quietly during the 20–30 minutes that the catches were made, and we could be reasonably sure that the figures obtained were a good indication of the individual's attraction. The results of five collections in the hot summer weather—low mosquito population—and one collection in the rainy season, when anophelines were very abundant, are recorded in Table I.

TABLE I.—*Distribution of A. albimanus Bites Among a Jamaican Negro Family at Ferry, Near Kingston, Jamaica*

	Sex and Age	Number of Bites Recorded	
		Summer Weather (5 Collections)	Rainy Season (1 Collection)
Mr. Bailey	M 36	103	199
Mrs. Bailey	F 30	25	49
Marjorie	F 9	23	40
Donald	M 8	45	61
George	M 5½	8	13
Thelma	F 5½	18	10
Malcolm	M 2½	18	15
Linette	F 1	0	2

These figures show that at this period the baby—Linette—remained almost completely free of bites, in striking contrast to the very great attraction of her father. Mr. Bailey attracted nearly three times as many mosquitoes as the eldest boy, over four times as many as his wife or eldest girl, over ten times as many as each of the three younger children, and over 150 times as many as the baby. The single catch in the rainy season—the period of greatest anopheline abundance—suggests also that at these high figures the adult male attracts a proportionately higher number of mosquitoes.

These observations were repeated on two Jamaican East Indian families in the same neighbourhood. The results are shown in Table II.

TABLE II.—*Distribution of A. albimanus Bites Among Members of Two Jamaican East Indian Families Near Kingston, Jamaica*

	Sex and Age	Bites Recorded (2 Collections)		Sex and Age	Bites Recorded (1 Collection)
Mr. Anderson	M 45	58	Mr. Williams	M 36	110
Mrs. Anderson	F 36	21	Mrs. Williams	F 24	43
Dorothy ..	F 15	13	Livette ..	F 7	6
Austen ..	M 6	6	Wilfred ..	M 4	13
Melvina ..	F 2	0	Marilyn ..	F 3	10
			Alphonse ..	M 14 mths.	2

These figures show the same general trend, the scarcity of bites on the two youngest members contrasting with the great attraction of the adult males. In both families, as with the Baileys, the adult women attracted less than half as many mosquitoes as their husbands.

In order to find out how far this striking difference in the distribution of anopheline (*A. albimanus*) bites applies during the night, when the family are asleep, observations were carried out on the Bailey family indoors during the half-hour before dawn. The six children were asleep on the single bed; Mr. Bailey sat near by, and Mrs. Bailey was absent. The results were as follows: Mr. Bailey, 81; Marjorie, 3; Donald, 13; George, 0; Thelma, 3; Malcolm, 1; Linette, 3.

The very great attraction of the adult male is again evident, with the eldest boy, as before, next in order of attraction. Particular attention was paid to mosquitoes attempting to bite the baby—Linette. Observations at sundown had already shown how extremely sensitive she was to mosquitoes even settling on her skin. In the pre-dawn observations it was interesting to note that even when she was asleep she was still very sensitive to mosquitoes attempting to bite. Those mosquitoes attracted to her spent a long time probing around, and when the mouth parts were finally inserted the mosquito was shaken off in each case before actual feeding could take place. In contrast to this, mosquitoes alighting on Mr. Bailey, and to a less extent on Donald and Marjorie, bit immediately after settling and took a blood meal with great rapidity. In this respect it is worth noting that many adults are quite unaware of anophelines feeding on them.

It is possible that the interrupted biting, so marked in the case of the baby, might apply to a certain extent to the next youngest member of the family—that is, to children 2 to 3 years of age. Plans to extend these observations, however, received a severe setback when, during my absence, the Bailey family was attacked by "vomiting sickness," from which Mrs. Bailey, Malcolm, Linette, and a premature child all died within a few days of each other.

During a four-weeks visit to Trinidad it was possible, thanks to the co-operation of Dr. H. P. S. Gillette and Major Senior White, to repeat the sundown observations on *A. aquasalis* and *A. bellator*, the two vectors of malaria in that island. Arrangements with suitable family groups were not easy to make at short notice, and repeats on exactly the same group were not possible. The results with *A. aquasalis* are given in Table III.

TABLE III.—*Distribution of A. aquasalis Bites Among East Indian Family Groups at Sundown. New La Paille, Trinidad. Three Collections*

	Sex and Age	Bites Recorded		Sex and Age	Bites Recorded
Buddhu..	M Adult	16 18	Hubert Knutt ..	M Adult	21
Mrs. Sukea	F ,,	6 —	Corisha Mohammed	F ,,	2
Ramnarin	M ,,	18 —	Earlyn Mareth ..	F 3½	1
Lochu ..	M 8	13 8	Chakra Mohammed	F 3	0
Sukdeo ..	M 3	1 2	Ethlina Mohammed	F 10 mths.	0
Sriprasad	M 2½	2 7			

Allowing for the absence of a baby in the first group, for the low degree of biting in the second group, and for the absence of repeats, the results suggest that the general trend of biting is not unlike that of *A. albimanus*.

The observations on *A. bellator* were much more satisfactory, as both family groups included a well-behaved quiescent baby, and there was a high degree of biting. The results of two collections are given in Table IV.

TABLE IV.—*Distribution of A. bellator Bites Among Two East Indian Family Groups. Cumuto, Trinidad*

	Sex and Age	Bites		Sex and Age	Bites
Sarah Mohammed..	F Adult	12	Pancham Ramprasad	F Adult	15
Ramjug Sooknanan	M 15	12	Teresa	F 14	13
Ramdad Sooknanan	M 13	17	Samdaye	F 10	28
Said Mohammed ..	M 5½	4	Chumania	F 8	9
Sahidan Mohammed	F 17 mths.	1	Chandramati ..	F 10 mths.	0

Again the scarcity of bites on the babies is in striking contrast to the greater attraction of the mother and the older children (the father of each family being absent).

These observations on Trinidad anophelines, incomplete though they are compared with those made in Jamaica, nevertheless indicate roughly the same general behaviour, and suggest that the uneven distribution of bites may be common to many other anophelines besides *A. albimanus*.

Discussion

What bearing have these facts on malaria transmission and epidemiology? The findings appear to have two quite different implications. First, the fact that the younger age groups—under 2 years of age—are bitten so seldom compared with older children and adults must confer a considerable degree of protection from infection, especially with a species like *A. albimanus*, which seems to have a very low infection rate. In the Bailey family, for example, repeated blood examinations over a period of about eight months failed to reveal any sign of malarial infection in the two youngest children, Malcolm and Linette. Thelma—aged 5½—also remained free of infection, while *Plasmodium falciparum* infections were recorded in George (5½), Donald (8), and Mrs. Bailey, and a persistent quartan infection in Marjorie (9). The absence of parasites in several tests on Mr. Bailey is presumably related to a fairly effective immunity built up over years of exposure to infection.

In this anopheline-infected district there were other families too in which some of the children appeared to have remained free of malarial infection during the first year or two of life. On the other hand, the freedom of the younger age groups from anopheline bites is relative only, and by no means absolute. With a high mosquito population these children may still be bitten many hundreds of times in the course of a year, and in this same area there were several records of *P. falciparum* infections during the first year of life. Bearing in mind the biting habits of *A. albimanus*, described above, it seems very likely that when infants do get infected it is from mosquitoes which bite them without extracting any blood, as it has been established that infection can result from the simple insertion of the proboscis (Boyd, 1949).

The second implication of these findings regarding the unequal distribution of bites and feeds in different age groups is that they may play an important part in determining which age group is mainly responsible for infecting anopheline mosquitoes with malaria parasites. A commonly accepted idea that young children form the main reservoir of malarial infection may need considerable revision, as it is strongly indicated that, other things being equal, the adult gametocyte carrier could be a much greater danger to the community because of the much greater frequency with which he is bitten; and this applies particularly to the men, who are much more attractive to anopheline mosquitoes than their womenfolk. Although the gametocyte rate of children under 5 years is usually higher than in older children or adults, not only are the youngest children bitten much less frequently but, equally important, the mosquitoes which do bite them seem to have much less opportunity of following the bite with a full blood meal.

This rather simplified interpretation of these new findings may of course require modification as new factors come to light. The direct comparison of gametocyte rates and gametocyte counts between different age groups is not necessarily an indication of the infectivity of these "carriers" to mosquitoes. Again, the tendency of the adult woman's immunity to break down during pregnancy (Walton, 1949) and to result in severe attacks of malaria (as happened with Mrs. Bailey in the family described above), might increase her importance as a potential mosquito infector.

In Jamaica several of these implications are being followed up to try to find out what part each age group of gametocyte carriers might play in maintaining transmission or initiating outbreaks, and it is hoped to communicate these results in due course.

It is tempting to speculate about the possibilities of African and Oriental anophelines showing the same biting trends as those studied in the Caribbean. Should these habits prove similar they would certainly help to explain some inconsistencies about infant infection rates in those regions. For example, malariologists in Africa have long been struck by the low rate of malarial infection in infants under 3 months, even in areas where the main vector—*A. gambiae*—is very abundant and maintains a gland infection rate of 10% or more. Explanations vary from an inherited immunity in the first few months of life to some purely mechanical protection from mosquito bites at that age. The whole subject of infant parasite rates in relation to exposure

to the bites of infected mosquitoes under these conditions has recently been discussed by Macdonald (1950), who points out that the only reasonable explanation of the discrepancy between observed and calculated figures is that the number of infective bites to which the infants are exposed must be less than that estimated.

In the great malaria epidemic of Ceylon in 1934–5 one of the most difficult features to explain was the explosive nature of the outbreak. During the early stages of the epidemic, outbreaks of sickness were mainly confined to adults, there being a remarkable absence of mortality among infants during the first four weeks at least. Gill (1938) has pointed out that if we attribute this outbreak to new infections rather than to a wave of relapses, it would be necessary to assume that at the beginning of the epidemic the main biting activities of *A. culicifacies* were directed towards adults. In the light of the observations described above this explanation now seems much more feasible.

Before these speculations about conditions in other countries carry us into deep water it will obviously be necessary to repeat these observations on their particular vector *Anopheles*. The possibility that this biting factor may also enter into problems of other insect-borne diseases can hardly be overlooked. Culicine mosquitoes appear to bite infants rather more readily than anophelines do, but no systematic observations have yet been done on them, and there should be many interesting possibilities in following up this line of inquiry.

Summary

Observations on the biting habits of *A. albimanus* on family groups in Jamaica have shown that babies are bitten much less frequently than older children or adults. Similar behaviour has been seen in *A. aquasalis* and *A. bellator* in Trinidad. This uneven distribution of bites and feeds has been discussed in relation to general problems of malaria transmission and epidemiology.

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Research on "agenized" flour is carried a step further by a note from a Nottingham group of research workers (*Nature*, May 12, p. 773) which describes how they were at first unable to produce convulsions in rabbits and traced this to the presence in the animal's diet of greenstuff, which seemed to protect against convulsive doses of the toxic substance. It will be recalled that flour is improved in keeping and baking quality by treatment with "agene" (nitrogen trichloride), and some time ago it was shown that flour treated in this way and fed to dogs and rabbits gave them fits. Medical Research Council workers were unable to produce any abnormal symptoms or signs in human beings given large amounts of the treated flour. The toxic substance was identified by chemists as a derivative of methionine, an amino-acid occurring naturally in the protein of the flour, and as little as 2 mg. would cause convulsions in a normal rabbit. A rabbit getting 150 g. of fresh greens a day, however, would be protected, or almost completely so. The reason for this is so far unknown. The toxic substance has been studied in the laboratory for its inhibitory effect on the growth of the bacterium *Leuconostoc mesenteroides*, an effect abolished by glutamine. Fresh greenstuff is often rich in glutamine, and it may be this which protects the rabbit.

BLACKWATER FEVER IN AFRICAN CHILDREN

BY

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The rarity of blackwater fever among indigenous African adults is well recognized (Fairley, 1946; Joyeux and Sicé, 1950; etc.). Sporadic cases do, however, occur, and larger numbers have been reported under special circumstances, as, for example, when adult Africans have migrated from non-malarial hill country to an endemic malarial area. This has been recorded in the Cameroons (Strong, 1944). Again, blackwater fever cases have been observed among groups of Africans who have been using either antimalarial suppressive drugs or mosquito-nets. Thus, Findlay (1949) noted a definite increase in cases among West African soldiers, who were taking no quinine, but who were being partially protected by mosquito-nets and mosquito control.

In addition, there would seem to be some unexplained geographical factor to be considered. Gelfand (1944) records that he has never seen a case of blackwater fever in an African, presumably referring to experience in S.E. Africa, and more particularly Southern Rhodesia. Shelley (1931), in a review of cases seen in Nyasaland between 1921 and 1930, makes no reference to the disease having occurred in Africans during this period. In contrast to this, cases occurring sporadically are noted occasionally in West African adults.

In normal circumstances blackwater fever is extremely unusual amongst indigenous African children, despite the fact that, during childhood and more especially infancy, severe attacks of subtertian malaria occur frequently, at least in Nigeria. However, as is mentioned by several authorities (Manson-Bahr, 1945; Maegraith, 1948), if the development of malarial immunity ("premunition") is interfered with—as, for example, by the repeated inadequate quinine treatment of malaria in childhood—blackwater fever can occur. Thus, Chesterman (1935) observed a case of blackwater fever in an African child aged 2½ years. There was a past history of occasional dosage with quinine for attacks of fever. The blood film showed *Plasmodium falciparum*. The illness was precipitated by the taking of quinine, and consisted of a single mild bout of haemoglobinuria, lasting only a day. Mackey (1928) recorded a case in Nigeria. This occurred in an Ibo child aged 2½ years. Again there was the same background of occasional treatment with quinine over a number of years. The blood film showed *P. falciparum* to be present. In this case a severe bout of haemolysis, with typical urine changes, was followed by increasing jaundice, unconsciousness, and death.

In contrast to these two reports, Jackson (1935) has described a case in an infant of 16 months in the Plateau Province of Northern Nigeria. The blood film showed *P. falciparum*. The onset of the illness was associated with the taking of quinine, but there was no definite history of previous quinine therapy.

Case 1

A Yoruba boy aged about 2 years was admitted to hospital at 6 p.m. on February 8, 1949. His mother, an ex-nurse of a fairly low standard of training, gave the following history. The child had always been delicate and had had fever frequently, sometimes as often as monthly. This had always been treated by the mother with a tablespoonful of quinine mixture, given for one or two doses on each occasion. About a week before admission a further attack of fever occurred, for which the mother gave a tablespoonful of quinine mixture. After this the child seemed improved until the actual day of admission, when the pyrexia recurred, together with a shivering attack, general malaise, and vomiting. A further tablespoonful of quinine mixture was given at about 10 a.m. At 4 p.m. the mother noticed that the child had passed about 8 oz. (230 ml.) of dark reddish-black urine.

On examination the child was obviously ill, with a temperature of 101° F. (38.3° C.) and a pulse of 104. The liver was enlarged one fingerbreadth, and the spleen was just palpable. Laboratory investigations:—(1) Urine: dark blackish-brown in colour, similar in appearance to strong Turkish coffee, and faintly acid; chemical tests for blood strongly positive; albumin +++; microscopical examination showed granular casts and debris ++; no red blood corpuscles seen. (2) Blood film: scanty ring forms of *P. falciparum* were present.

Treatment was begun with phenobarbitone, ¼ gr. (16 mg.) twice daily for three days, and proguanil, 100 mg. twice daily for 10 days. Haemolysis continued for just over 36 hours, the urine changing gradually from a Madeira-wine colour to a dark yellow. The child developed bronchopneumonia on the fourth day after admission; this responded rapidly to a seven-day course of procaine penicillin (1 ml. intramuscularly daily). On discharge on February 20 the patient seemed to have made a complete recovery, although the haemoglobin was only 75%. An oral iron mixture was prescribed and the mother was advised to keep the infant on permanent proguanil prophylaxis.

Case 2

A Yoruba boy aged about 2½ years was admitted to hospital on December 19, 1949. His mother, the wife of a schoolmaster, gave the following history. For the previous 15 days the child had been ill with fever and a slight cough. Treatment with various non-specific remedies had been tried by the parents. On the day before admission the child had been given two tablespoonfuls of quinine mixture on two occasions. (The patient, who had had frequent attacks of "fever" in earlier infancy, had often been treated with short courses of quinine for a day or two.) At 9 a.m. on the day of admission the mother noticed that the child was passing urine "like blood."

On examination the child did not seem to be seriously ill. There was a slight anaemia. The liver and spleen were not palpable. The temperature was 100.6° F. (38.1° C.) and the pulse 120. Laboratory examinations:—(1) Urine: reddish-brown in colour, similar in appearance to angostura bitters; chemical tests for blood strongly positive; albumin +++; microscopical examination showed deposit of mainly unidentifiable debris; no red blood corpuscles observed. (2) Blood film: very occasional ring forms of *P. falciparum* seen. (3) Haemoglobin 60%.

Haemolysis stopped after about 24 hours, and the urine cleared rapidly. Treatment with phenobarbitone, ¼ gr. (8 mg.) four times daily for three days, and mepacrine, 0.05 g. twice daily for seven days, was started on admission. The temperature returned to normal after two days. Convalescence was uninterrupted. Treatment with oral iron was given for the anaemia. The mother was advised to begin permanent proguanil prophylaxis.

Case 3

A 6-year-old Yoruba boy was admitted to hospital on April 3, 1950. He gave a history of having had fever for three days. There was no history of his having taken native medicine or having been bitten by a snake. On the morning of the day of admission he had noticed that his urine was dark. He gave a history of having had a similar type of illness some two years before.

Examination showed an anaemic child with a temperature of 104° F. (40° C.) and a pulse of 114. The liver was enlarged two fingerbreadths and the spleen three fingerbreadths. Laboratory investigation:—(1) Urine: port-wine colour; slightly alkaline; chemical tests for blood strongly positive; albumin +++; microscopical examination showed cellular debris in abundance; no red blood cells; granular casts ++. (2) Blood films (on three occasions): no malarial parasites present. (3) Haemoglobin, on April 4, 55%. (4) Examination for sickling showed no evidence of this after 24 hours.

Treatment was begun with mepacrine, 0.1 g. twice daily, and oral iron. Haemoglobinuria continued for about two days, the urine clearing rapidly after this. The boy was discharged on April 13.

Case 4

A 5-year-old Yoruba boy was admitted to hospital on April 27, 1950. The father, a clerk, gave the following history. The patient had had numerous attacks of fever during earlier childhood; these had often been treated with short courses of quinine. The present illness began four days before admission with a further bout of fever, for which the father gave a dose of about 1 oz. (28 ml.) of quinine mixture. In the evening of the day before admission the child had been passing dark-coloured urine, which had continued up to the time of admission. He had vomited once.

On examination the patient showed a definite icterus and anaemia. The liver was not palpable. The spleen could just be felt. The temperature was 99.8° F. (37.7° C.) and the pulse 110. Laboratory investigations:—(1) Urine: dark brownish black in colour; chemical tests for blood strongly positive; albumin +++; microscopical examination showed no red blood cells; granular casts +; unidentifiable debris +. (2) Blood film: scanty rings of *P. falciparum*. (3) Haemoglobin 60%.

Treatment was started with proguanil, 100 mg. thrice daily for seven days, and phenobarbitone, ¼ gr. (16 mg.) thrice daily for five days.

Haemoglobinuria continued on the morning of April 28. The child had become delirious, and was obviously severely anaemic and markedly icteric. The pulse was 130. A blood transfusion was refused by the parents. At 6 p.m. the haemoglobinuria had stopped, but the child had become comatose, with a feeble thready pulse (about 150 a minute). He died in the early hours of April 29.

Discussion

It will be noticed that in three of these cases there was a definite history of occasional dosage with quinine during earlier childhood, the actual haemolytic crises following the last doses of quinine. The parents were all of an educated type—that is, ex-nurse, schoolteacher, clerk. The incidence of blackwater fever in Europeans in Nigeria has dramatically fallen in the last few decades. This is indicated by the fact that in 1948 only two cases were recorded, both of which recovered (Nigeria, 1950). In addition, it must be remembered that this fall has occurred despite a very great increase in the European population. The most probable main explanation of this decline is that regular prophylaxis

with antimalarial drugs is now carried out almost automatically by most of the European population.

In contrast to this it seems not unlikely that blackwater fever may in the near future occur with increasing frequency amongst the educated African population, especially the children. Antimalarial drugs are increasingly easy to obtain, and skilful advertising in the cinema, press, and shops will certainly make new African converts to malaria chemotherapy. The danger lies in the likelihood that in many cases chemoprophylaxis will not be continuous—either because the desirability of this may not have been appreciated or for financial reasons. If this is so, the African child in a hyperendemic zone will neither be adequately protected from malaria nor be able to build up immunity to it. A similar situation may be produced by the repeated casual treatment of all fevers in African infants with inadequate doses of antimalarial drugs. This may be overstating the case, as the most likely offender —quinine—is being to a certain extent ousted by the synthetic antimalarials mepacrine and proguanil. However, quinine is still sold very widely, and blackwater fever has been described after mepacrine. Blackwater fever after proguanil does not seem to have been recorded. It must be mentioned, however, that proguanil has been in use for only a few years, and then during the period when the importance of the regularity of prophylactic dosage has been very widely accepted and put into practice.

In the paediatric out-patient department in Ibadan only intelligent educated mothers who can afford it are advised to give their children malarial chemoprophylaxis in the form of proguanil. In addition, it is stressed to them that this must be an uninterrupted process and, indeed, should continue throughout life, as otherwise there is a definite danger that the pernicious manifestations of subtertian malaria—that is, cerebral malaria, etc.—may occur in adult life. It is realized that not all authorities would agree with this advice, as they feel that the "normal" process of repeated infection with subtertian malaria that occurs in almost all African children in a hyperendemic zone is inevitable and not such a serious matter as is usually suggested. This has been stressed by the work of Garnham (1949) in the Luo tribe of Kenya and by Swellengrebel (1950) in the African population (Cimarons) of a village in the interior of Surinam. Both authors note that, despite an almost universal infection with *P. falciparum* during infancy and childhood, only a very small mortality, or even morbidity, is attributable to malaria in these areas. It seems unlikely, though admittedly statistically unproved, that similar conditions pertain in Nigeria, where severe and often fatal pernicious attacks of subtertian malaria are seen comparatively frequently in young children and appear to represent the price paid for the development of malarial immunity in the surviving majority.

Summary

The rarity of blackwater fever in Africans, especially in childhood, is discussed. Four cases occurring in Nigerian children are recorded.

The fall in incidence of blackwater fever in the European population of Nigeria is noted.

The possibility of an increase in the number of cases of blackwater fever in the children of educated Africans, following the wider casual use of antimalarial drugs in the home, is considered.

In view of this danger it is advised that only intelligent educated mothers should be advised to give their children chemoprophylaxis—in the form of proguanil. The desirability of continuing this into adult life is mentioned.

My thanks are due to Professor Alexander Brown, Department of Medicine, University College, Ibadan, for permission to publish this article.

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LABORATORY DIAGNOSIS OF URINARY-TRACT INFECTIONS

WITH SPECIAL REFERENCE TO LACTOSE-FERMENTING COLIFORM STRAINS

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The common infecting agents in disease of the urinary tract are organisms of the coliform group. This is a group of immense complexity, and a prolonged bacteriological analysis is necessary before any one member can be accurately described. It is therefore common routine practice to disregard these minor differences and describe them by some all-embracing term such as *Bact. coli* (Ainsworth–Davies, 1950) or simply as "coliform bacilli." It is the purpose of this paper to show that the subdivision of the group into true *Bact. coli* and *Bact. aerogenes* species, and a group containing all other lactose-fermenting Gram-negative bacteria to be called "atypical strains of the coliform group," may be of practical importance. A simple means of achieving this is described, utilizing only information obtainable in 24 hours. The results obtained by this method have been compared with those from one of the standard longer techniques. The data have also been analysed to see if they show any correlation between the nature of the infecting strains and the pathology of the lesions.

The incidence of a variable proportion of *Bact. aerogenes* strains in these infections has many times been reported, and recently attention has also been drawn to the sulphonamide insensitivity and penicillin sensitivity of large numbers of coliform organisms. The fact that nearly all are sensitive to streptomycin and to some of the newer antibiotics (Frank *et al.*, 1950) in no

way detracts from the topical importance of these observations, since it is still routine practice to treat most cases with a sulphonamide on first diagnosis. Furthermore, resistance to streptomycin may rapidly develop, and no new antibiotic is generally available in this country for the treatment of these infections.

Material

Considerable difficulty was experienced in deciding what constituted a urinary-tract infection in the absence of a definite urological diagnosis, and, since clinical diagnosis was frequently made on the result of the laboratory findings, there was in retrospect often little independent evidence.

Numerous authors have shown that contamination occurs in a very high percentage of routinely collected urines, even catheter specimens. There is a considerable probability that even with rigorous precautions as many as 10% of urines may grow organisms the presence of which is not attributable to any discoverable pathological lesion. In a preliminary study of 200 specimens primarily conducted to confirm that there was satisfactory correspondence between wet-film and dry-film diagnosis a large number of contaminated specimens, mostly containing cocci, were in fact noted. Cystoscopic and ureteric specimens were only rarely contaminated, which fact emphasizes the importance of collection technique. Only undoubted cases, therefore, in which there were micro-organisms and a definite excess of pus cells in the centrifuged deposit, and, with one exception, relevant clinical findings, have been accepted as providing infected as opposed to contaminated urines. It is felt that there is need for a critical review of the characters of a urinalysis that constitute grounds for the diagnosis of a urinary-tract infection, and particularly of the significance of albumin.

Cases.—The patients were all the 86 cases with urinary-tract infections in the wards of Guy's Hospital from whom specimens had been sent to the Department of Clinical Pathology for examination, and 51 others in whom the urinary tract was thought to be normal and from whom the contaminating strains studied were derived. Only those patients from whom a lactose-fermenting coliform strain was isolated have been included, but they were otherwise unselected. The specimens were received during the months of November to May; all had been collected by students and nursing staff. Only catheter specimens were accepted for culture from female patients, and from the male patients 18% were catheter specimens and 82% were interrupted mid-stream urines collected with due precautions to avoid contamination.

Strains.—From primary growths on MacConkey plates 165 strains were obtained. When the growth looked pure a representative colony was picked and when more than one organism appeared to be present one of each type was investigated. Of these 165 strains 114 were considered to come from the true cases of infection and 51 to be contaminating urines from the cases that were not clinically infected. Not all contaminants encountered in the latter part of the investigation were studied.

Methods.—All cultural methods were those described by Wilson and Miles (1946). O'Meara's modification of the Voges–Proskauer reaction is found in this department to be more generally useful than Barritt's. All investigations were performed shortly after first isolation.

Penicillin sensitivities were determined in tubes containing 5 ml. of glucose broth with 100 and 20 units per ml. and a control tube. For sulphonamide sensitivities the plate method of Harper and Cawston (1945) with a control plate was employed. The inocula were standardized by the method in use at the Army Vaccine Laboratory (Sayers, 1949; personal communication to J. B. E.), which consists in emulsifying in peptone water the inoculum on a 3-mm. loop, flaming the loop, touching the emulsion with it, and then agitating the loop in a fresh tube of peptone water. This loop is then used for inoculation, and on solid media invariably produces separate colonies. The gas-production test was carefully standardized so that the temperature within the medium—lactose bile salt broth—was 44° C ± 0.5.

Classification of Strains

An attempt was made to apply the Ministry of Health (Report, 1934) classification of coliform strains met with in water in Great Britain.

Table Showing the Number of Strains in Each Type in the Ministry of Health Classification and the Number of Strains in Each Broad Group in Relation to the Lesions from which They Were Isolated

Source of Strains	No. of Cases	No. of Strains	*Bact. coli*		Atypical Coliform Strains						*Bact. aerogenes*	
					Intermediate Strains		Irregular Strains					
			Type I Faecal	Type II	Type I	Type II	Type I	Type II	Other Types Producing Gas at 44° C.	Other Types Not Producing Gas	Type I	Type II
Infected urinary tracts	86	114	57	11	10	6	2	5	6	9	6	2
Normal urinary tracts	51	51	17	4	11	2	4	1	6	1	4	1
Total strains		165	74	15	21	8	6	6	12	10	10	3
			Bact. coli		Atypical Coliform Strains						*Bact. aerogenes*	
Infected urinary tracts			68 (60%)		38 (33%)						8 (7%)	
Normal urinary tracts			21 (41%)		25 (49%)						5 (10%)	
Total strains			89 (54%)		63 (38%)						13 (8%)	
Cases of pyelitis	34	47	31 (66%)		14 (30%)						2 (4%)	
Cases of cystitis:												
Female	8	11	9 (82%)		2 (18%)						0	
Male	5	8	3 (38%)		3 (38%)						2 (24%)	
Cases of organic obstruction	9	9	3 (33%)		5 (56%)						1 (11%)	
Cases with a neurological lesion	3	5	5(100%)		0						0	
Cases with some structural pathology of urinary tract	24	30	17 (57%)		10 (33%)						3 (10%)	

Out of a total of 165 strains, 22 (12.1%) were not classifiable into any one of the eight groups, and six strains of otherwise typical *Bact. coli*, Type I faecal, did not give a positive methyl-red reaction after three days in glucose-phosphate medium at 37° C. This is a very high proportion, and raises the question of the applicability of this classification to pathogenic organisms—an application it presumably was not designed to have.

When the unclassifiable strains are further examined two groups can be identified, each containing in this series as many strains as or more strains than the three standard types—Irregular Types I and II and *Bact. aerogenes* Type II. The first of these groups consisted of six strains that produced gas at 44° C. but were otherwise typical *Bact. aerogenes*, five being indole-negative and one indole-positive; the second group consisted of seven strains that produced no positive reaction in any of the fluid test media. This latter group was not homogeneous in its other characters. Of the remaining nine strains five liquefied gelatin after varying periods of time but had no other common characteristic, and the remainder was a miscellaneous group. No example of *Bact. coli* Type I failing to produce gas at 44° C. was encountered.

If the intermediate and irregular strains are grouped together they are nearly as numerous as the *Bact. coli* group and five times as numerous as the *Bact. aerogenes* group. This is the grouping that has been used in attempting to correlate types of lesion with their bacteriology and also with the drug sensitivity of the infecting strains.

The time taken in determining the type in the Ministry of Health classification also renders it inapplicable to routine diagnosis. Accordingly those individual reactions used in the classification the results of which may be available in 24 hours, and the appearances of the primary cultures, have been separately correlated with these characters.

44° C. Gas-production Test

Twenty-four-hour readings have been used throughout, as they are the ones that will be available for routine diagnosis, and, in fact, of the first 104 strains none failed to form gas in 24 hours yet did so after 48 hours. On this basis 95 strains produced gas and 70 did not. Of the gas-producing strains 91% showed some sensitivity to penicillin against only 41% of the other strains. The comparable figures for sulphadimidine are 94% and 51% respectively. Both these differences are significant. The behaviour of the strains isolated from infected and contaminated urines was essentially similar. Only 26% of strains that did not produce gas were sensitive to what may be regarded as therapeutic levels of sulphadimidine in non-urinary infections (up to 10 mg./100 ml.).

Performance of the Gas-production Test on the Centrifuged Deposit.—In order to make an early report as informative as possible it is clearly desirable to have the result of this test at the same time as the plate is read. This could be achieved if it were practicable to perform it directly from the specimen. The centrifuged deposits from 48 urines were therefore used as inocula and the results corresponded well with those subsequently obtained from the plate cultures. In order to minimize routine work, it is suggested that this procedure might be performed only on those deposits in which both pus cells and bacilli are seen. On this plan only one discordant result was obtained—that of the primary test being positive while the test performed on what was apparently a pure culture gave a negative result. In such cases the probable mechanism is that a small number of faecal coliforms which are colonially indistinguishable give a falsely positive result. It seems that such cases will be uncommon, perhaps because of the smaller percentage of *Bact. coli* among contaminating strains (See below).

Mucoid Appearance of the Colony

It is well known that some aerogenes strains will, under certain conditions, give a highly typical appearance of gelatinous semi-confluent growth. Mucoid but discrete colonies, on the other hand, although shown by this type, are not confined to it. In all there were 27 strains showing an obviously mucoid colony at 24 hours, 11 of which produced gas at 44° C. Another 17 strains produced an equivocal appearance and have not been further considered. Eight of 89 (9%) *Bact. coli* strains and 7 of 13 *Bact. aerogenes* (54%) were mucoid. There is some correlation between the mucoid characteristic and resistance to 100 u./ml. penicillin although not to sulphonamide. If the strains that are both unable to produce gas and are mucoid are considered it then appears that of 12 strains 7 (58%) are resistant to 100 mg. sulphonamide and 11 (92%) are resistant to 100 u./ml. penicillin. No such strain is either sensitive to 10 mg. sulphonamide or 20 u./ml. penicillin.

Haemolysin; Gelatin Liquefaction

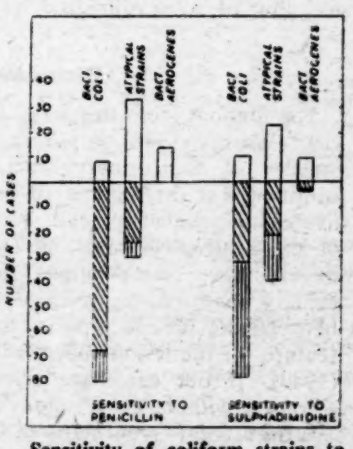
From the first 104 strains examined subcultures were made on to 5% horse-blood-agar plates. It was found that approximately one in three of each type was haemolytic and that this ratio was closely similar in groups of both infecting and contaminating strains. Subsequently the test was not performed.

Only five strains possessed this ability, and none of them was a true *Bact. cloacae* strain. There was no correlation with either the type of the lesion or the sensitivity.

Relation of Strains to Drug Sensitivity

It will be seen from the accompanying Chart that, although the majority of organisms show some sensitivity to both penicillin and sulphadimidine as many as 54 (33%) are insensitive to 100 u./ml. of penicillin. Forty-two (25%) are insensitive to 100 mg./ml. sulphadimidine, and only 64 (39%) are sensitive to ordinary therapeutic levels.

In general, *Bact. coli* strains are sensitive to urinary concentrations of both penicillin (81/89 = 91%) and sulphadimidine (79/89 = 89%), whereas the *Bact. aerogenes* strains are not, four



Sensitivity of coliform strains to 20 u./ml. penicillin and 10 mg./100 ml. sulphadimidine (vertical hatching) and resistance to 100 u./ml. and 100 mg./100 ml. (plain columns). Oblique hatching shows intermediate degrees of sensitivity.

being sensitive to sulphonamide and none to penicillin out of 13.

The atypical coliform strains occupy a position intermediate between the other two groups in this as in other respects (30/63 = 47% penicillin-sensitive and 40/63 = 63% sulphonamide-sensitive).

Relation of Type of Organism to Pathological Features of Lesion

With the exception of pyelitis the number of patients suffering from any one condition is small, but it is possible to group the lesions so that some significant relationships emerge. There is a significantly lower incidence of *Bact. coli* in lesions complicated by organic obstruction (33%) than in pyelitis (66%), as an example of a non-obstructive lesion (difference = 33%, standard error (S.E.) of difference = 16%), and the difference remains significant if the analysis is confined to male cases (difference = 50%, S.E. = 21%). There is also a just significant difference when the obstructive cases (33%) are compared with the remaining infected cases (63%) (difference 30% ; S.E. 15%). It is remarkable, in view of the smallness of the groups, that there are significantly fewer *Bact. coli* in the male (38%) than in the female cases (82%) of cystitis (difference 44% ; S.E. 21%). No such difference was seen in pyelitis nor between cases of pyelitis in pregnant and non-pregnant women. No other significant correlations have been discovered between organisms and lesions, but the number of *Bact. coli* is significantly higher in all infecting strains taken together (60%) than in the contaminating group (41%)—a difference (19%, S.E. = 9%) which is referred to in the discussion.

Cases from which More than One Strain was Obtained

From 22 cases more than one positive culture was obtained. In only 10 of these were the strains of the same type, and it is perhaps worth comment that of five cases of pyelitis from which the same organism was twice obtained it was *Bact. coli* Type I in all. However, in three of the other five cases of pyelitis from which more than one strain was obtained none was of this type.

No definite evidence of change of sensitivity to either penicillin or sulphadimidine was obtained.

Discussion

The findings from this series lend little support to the view (Warner, 1948) that *Bact. aerogenes* is a common invader of the urinary tract, although it must be admitted that the number of neurological and obstructive cases included is small. With the possible exception of the obstructive cases, as opposed to those which merely have some other non-inflammatory genito-urinary abnormality, we have not found the correlation between the precise type of organism and the clinical features of the lesion suggested by Coleman and Taylor (1949). If our cases are classified as were theirs, in Group I, without gross lesions of the urinary tract, 65% are *Bact. coli* (43/66) ; and in Group II, of cases with a surgical or medical lesion, *Bact. coli* are again 65% (22/34). Owing to different methods of presenting results, the relevant literature, mostly referred to in these two papers, is not susceptible to bulk analysis, but we have gained the impression that it leaves this question as open as do our results.

A general differentiation into true *Bact. coli* and the Intermediate-aerogenes-cloacae Group of Wilson and Miles (1946) does, however, possess some clinical and therapeutic applications. It may also be of value in deciding whether a given strain is a pathogen or a contaminant. For routine work such differentiation is best achieved by a careful consideration of colonial appearances and the result of a gas-production test performed on the centrifuged deposit. With this information it is probably justifiable and of value to report the gas-producing non-mucoid strains as *Bact. coli*, the mucoid strains not producing gas at 44° C. as *Bact. aerogenes*, and all others as atypical *Bact. coli*. In this series the percentages then become: *Bact. coli*, 46% ; *Bact. aerogenes*, 8% ; and atypical strains, 46% — the differences between these figures and those in the Table being largely due to inclusion of the mucoid strains of *Bact. coli* among the atypical strains. This merely increases slightly the number of uninformative descriptions while being in no way misleading, and more than half the reports would still carry useful information otherwise not presented.

The relative infrequency of faecal *Bact. coli* and the high proportion of atypical strains among contaminants is at first surprising. It is, however, common laboratory experience that lactose-fermenting organisms presumed to be contaminants often do not "look like" true *Bact. coli* ; and Payne (1949) has shown that these organisms have in fact a short survival time on the skin. This evidence, with that of the rarity of contamination of operating-theatre specimens (Stephens and Enticknap, 1951) and the knowledge that very careful skin-cleansing will do much to eliminate extraneous organisms (Leishman, 1939), explains, in part at least, this finding.

Our sulphonamide and penicillin-sensitivity findings correspond with those of other workers. When these are examined together it is found that of 42 sulphadimidine-resistant strains only two are sensitive to 20 u./ml. and six to 100 u./ml. of penicillin. Thus the sensitivities to the two drugs appear largely to run parallel, and failure of treatment with sulphonamide implies a high degree of probability that penicillin treatment will also fail. In view of the almost universal sensitivity of coliform organisms to streptomycin it does not seem profitable either to investigate their behaviour in relation to penicillin or to exhibit it therapeutically, unless for its action on organisms other than coliforms.

It is clear that *Bact. aerogenes* infections will not respond to sulphonamide treatment, and it is unlikely that half of the infections due to atypical strains will. The outcome of the remaining cases due to strains of intermediate sensitivity is less apparent. The significance of the laboratory finding of sensitivity to high drug concentration, although discussed in its theoretical aspects by Warner (1948), has, so far as we are aware, yet to receive specific evaluation. To obtain clear-cut results of therapeutic and prognostic significance large numbers of cases will require to be analysed because of the numerous independent variables inseparable from routine clinical practice. The method here described is applicable to such a large-scale survey, and with it it is hoped to obtain further information on this and the other points referred to above.

Summary

One hundred and sixty-five strains of lactose-fermenting coliform organisms isolated from contaminated and infected urines have been studied, and an attempt has been made to derive from them a simple classification suitable for routine reporting.

The need for such a simple but informative description based on the data available at the end of 24 hours is stressed, and the unsuitability of the Ministry of Health classification for this purpose is demonstrated.

A routine method for reporting *Bact. coli*, atypical coliform strains, and *Bact. aerogenes* is described, and the significance of this grouping in relation to the penicillin- and sulphonamide-sensitivity is discussed.

No correlation between the type of organism and pathology of lesion, with the possible exception of purely obstructive lesions, was found in this series.

We wish to thank Dr. F. A. Knott and Professor R. Knox for their helpful advice and criticism.

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Medical Memoranda

Two Cases of Locked Twins

The occurrence of the complication of locked twins on two occasions within six weeks is thought to be sufficient reason for reporting this rare event. The cases are of interest because they would seem to support a theory of causation put forward by Lawrence (1949).

Case 1

A primigravida aged 22 was referred to hospital on June 15, 1949, with a diagnosis of breech presentation. She was in the 34th week of pregnancy; the size of the uterus was compatible with the period of gestation, and there was no evidence of toxaemia of pregnancy. The foetal heart could be distinctly heard at two separate points, and the presence of twins was confirmed by *x*-ray examination. The leading foetus presented by the breech and the second by the vertex. Radiological examination of the pelvis showed it to be of the gynaecoid type, the true conjugate being 12 cm.

The further course of pregnancy was uneventful, and the patient was admitted to hospital at 7.30 a.m. on June 29, with the history that labour pains had begun four hours previously. Examination revealed the fundus uteri to be at the level of the ensiform cartilage, and strong contractions were palpable at intervals of ten minutes. There was no evidence of toxaemia of pregnancy, and, as rectal examination showed the cervix to be half dilated, sedation was secured with pethidine hydrochloride, 200 mg. At 2.30 p.m. the membranes ruptured, and twenty minutes later the breech was seen presenting at the vulva.

Pudendal block anaesthesia was carried out with 1% procaine, and when the breech distended the perineum a right medio-lateral episiotomy was performed. The foetus was delivered spontaneously to the inferior borders of the scapulae, and at this level further progress ceased. Examination showed that the head of the second twin was impinging on the neck of the leading one, the head of which was still above the pelvic brim. Under deep general anaesthesia, the head of the second twin was pushed up out of the pelvis and the leading twin delivered by manual extraction. It was found to be a macerated stillborn female child, 17 in. (43.2 cm.) in length and weighing 3 lb. 15 oz. (1,786 g.). As the second foetal heart could not be heard with certainty, internal version was performed and the second foetus delivered by manual extraction. It also was stillborn, and was 16 in. (40.6 cm.) in length and weighed 3 lb. 10 oz. (1,664 g.). Brisk haemorrhage ensued, and the single placenta was manually removed. It was found to have multiple areas of white infarction over two-thirds of its surface. There were two amniotic sacs and one chorion.

Recovery was uncomplicated, and the patient was discharged ten days after delivery.

Case 2

A primigravida aged 25 was referred to the hospital with a diagnosis of plural pregnancy on July 25, 1949. She was then in the 34th week and there was no evidence of toxaemia of pregnancy. Radiological examination confirmed the diagnosis of twins, presenting breech and vertex. The pelvis was of the gynaecoid type, the true conjugate being 12.25 cm.

On August 23 the patient was admitted to hospital, as signs of toxaemia of pregnancy had developed. Her condition improved with rest in bed.

At 12.15 a.m. on September 9 labour pains began and soon very strong contractions were palpable at regular intervals. She was given pethidine hydrochloride, 100 mg., and scopolamine, 1/150 gr. (0.43 mg.), at 4 a.m., when the contractions were recurring at intervals of five minutes. At 6.40 a.m. the membranes ruptured, and at 7 a.m. the breech presented at the vulva. Spontaneous delivery of the foetus ensued to the level of the axillae, when progress ceased. Under cyclopropane anaesthesia the arms were brought down, but the foetus could not be further delivered. Examination showed that the head of the second twin had entered the pelvis with the neck of the first one, the head of which was still above the pelvic brim. The head of the second twin was disengaged and pushed out of the pelvis, and the leading twin delivered by manual extraction. It was a stillborn macerated male child 16 in. (40.6 cm.) in length and weighing 3 lb. 12 oz. (1,700 g.).

Further examination now revealed that the cervix was dilated only to a diameter of four fingerbreadths, and, as the foetal heart was satisfactory, it was not considered necessary to interfere with the course of labour. The second child was delivered spontaneously at 9.5 a.m. in the occipito-posterior position. It was an active male child, 19 in. (48.26 cm.) in length and weighing 6 lb. 10½ oz. (3,019 g.). The single placenta was expelled 20 minutes later; there were two amniotic sacs and one chorion. Recovery was uneventful, and the patient was discharged on the tenth day after delivery.

Comment

The occurrence of locked twins is a rare event: the incidence given by Munro Kerr and Chassar Moir (1949) is 1 in 90,000 deliveries. Several factors have been suggested as causal agents in the production of this complication—namely, small foetuses, large pelvis, deficiency of liquor amnii, mono-amniotic twin pregnancy, and extension of the leading head.

Nicholson (1942) reviewed the causes and put forward the view that, while such predisposing factors might be necessary forerunners to locking, the actual combination of circumstances initiating the mechanism was fortuitous. Lawrence (1949) made a study of available case histories with a view to assessing the frequency of

the factors associated with twin-locking. He found the complication was more likely to arise if the pregnancy occurred in a primigravida and the uterine contractions were strong. He therefore deduced that the effective causal factor in the production of this complication was strong contractions in a uterus whose basic tone was high.

The cases reported bear out Lawrence's findings with regard to the incidence of locking, as both patients were primigravidae and in each case the uterine contractions were strong. Breech and vertex presentation, with the type of locking described above, is classed Group 2 by Lawrence, and in this group it is seen that 86.6% of the leading twins are stillborn. Another possible aetiological factor may, however, be suggested—namely, intrauterine death, when the flaccid dead foetus may be pushed past the head of the other twin by the expulsive force of a strongly contracting uterus.

Acknowledgments are made to Mr. J. T. Mair for advice and help.

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Cutaneous Anthrax in Dar-es-Salaam

It is interesting to note how this disease, once regarded with good reason as highly dangerous, has become progressively less serious so far as mortality figures go. Legge (1905) mentions a mortality rate of 25.6% in 261 cases, and states that this was a general average, though individual series might show better results. For example, Guy's Hospital from 1896 to 1904 had a mortality of only 7.1% in 56 cases, using treatment by excision or ipecac. Murphy *et al.* (1944) mention that the figures for West Virginia (U.S.A.) were 26.8% out of 394 cases in 1928–32 and 13.8% out of 390 cases in 1938–42.

In Britain, anthrax infections have become rarer, probably owing to the careful control of hides, which are the main source of infection. Holgate and Holman (1949) collected eight cases in 14 months from two tanneries in Leeds and district dealing mainly with hides from East and West Africa. Dar-es-Salaam is the main channel of export of hides from Tanganyika, and indeed from East Africa, and anthrax is endemic; it would be expected that, if some of these hides are infected, cases would occur among hide porters. Cutaneous anthrax does in fact occur quite often. In 1949, 28 cases were admitted to the infectious diseases section of the Dar-es-Salaam hospitals, and in the first seven months of 1950 there were another 27. Cases have not been found in other occupations.

Clinical Aspects

Diagnosis was frequently made by the men themselves. Appearances were typical, showing vesiculation surrounding a necrotic centre, and underlying oedema. Sometimes only a single moderate vesicle was seen, so quick are some to report. Owing to their black skin the colour changes of the inflammation were invisible. Severe spreading oedema seemed to occur mainly where the lesion was on the face or neck.

These men wear a minimum of clothing, therefore all parts of the body may be infected, some regions more frequently than others: face, 15; head and neck, 8; shoulders and upper arm, 12; forearm and hand, 6; chest, 7; back, 7; thigh, 3; abdomen, 1; more than one site, 4.

Bacteriological confirmation by examination of Gram-stained film was carried out, but not culture. In all except three cases the typical large straight Gram-positive bacillus was found.

Constitutional disturbance was not severe in most cases, the patients neither complaining of nor showing marked signs. As, however, some of these men do not complain lightly, it was thought that the highest temperature reached might be a better index of the toxaemia: The temperatures observed were: no fever or under 99° F. (37.2° C.), 18 cases; 99°–101° F. (38.3° C.), 16; 101° F. and above, 18. Three others were admitted unconscious, delirious, and collapsed, and died within two hours, demonstrating that cutaneous anthrax, if neglected, can be dangerous.

Treatment

During 1949 the standard treatment was with sulphathiazole, 2 g. on admission and 1 g. four-hourly. This was continued for four to seven days. Penicillin was used in addition towards the end of the year, when it seemed that the lesions resolved quicker and fever or toxaemia disappeared more rapidly. During 1950 soluble penicillin, 50,000 units three-hourly, was used in combination with sulphathiazole and continued for three to seven days. Scrutiny of the figures does not yield any statistical proof of the superiority of this regime, but clinically there was no doubt. Oedema and activity disappeared more rapidly, and the average duration of fever was 2.5 days in 1950, as compared with 3.4 days in 1949. Dressing with an antiseptic ointment held in place by "elastoplast" was the only local treatment.

Of the three fatal cases—two in 1949 and one in 1950—no history could be obtained about the duration of the infection, but from appearances it was probably at least a week.

No case remained seriously ill for more than 48 hours. In spite of treatment the ulcers were slow to clean up and heal, the average time for the slough to separate and the ulcer to become clean being 14 days, and another 10 days at least were required for full healing. This was noted because the policy was to retain the men until they were completely healed, as they are extremely slack in attending as out-patients.

They all returned to their work without anxiety. Second infections have not been noted.

My thanks are due to the Director of Medical Services, Tanganyika, for permission to publish.

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Reviews

THE VIRUSES

Handbuch der Virusforschung. By Professor R. Doerr and Professor C. Hallauer. Second Supplementary Volume. (Pp. 425; illustrated. £5 11s.) Vienna: Springer. 1950.

The Pathogenesis and Pathology of Viral Diseases. Edited by John G. Kidd. Symposium held at the New York Academy of Medicine, December 14 and 15, 1948. (Pp. 235; illustrated. £1 12s. 6d. or $5.) New York: Columbia University Press. London: Geoffrey Cumberlege. 1950.

An Introduction to the Study of Viruses. By Kenneth M. Smith, F.R.S. (Pp. 106; illustrated. 10s. 6d.) London: Sir Isaac Pitman and Sons. 1950.

These three books are designed to appeal to three different groups of readers: the *Handbuch der Virusforschung* to the expert on viruses, the symposium edited by Dr. Kidd to the expert in related biological fields, and Dr. Kenneth Smith's little book to a wider public who desire to know, or feel that they ought to know, "something" about viruses.

The *Handbuch* was first published in two volumes in 1938 and 1939. A supplementary volume appeared in 1944, and the present work is a second supplementary volume. The work consists of a number of articles written either in German or in English by different authors, sometimes in collaboration. The aim throughout has been encyclopaedic, and the writers chosen to deal with each topic are so clearly leaders in their own field that the articles may be accepted as authoritative.

It might be supposed that in so rapidly expanding a subject as virus research such review articles can be of only ephemeral interest. But it is surprising how often the laboratory worker still turns to the two volumes of the *Handbuch* published before the recent war. One of the great advantages of publishing reviews in works of this character rather than in the pages of the specialized journals is that in the *Handbuch* it is possible to illustrate the articles on a most lavish scale. The value of such expansive treatment is clearly seen in the section by Dr. Ruska on electron microscopy. Other articles on technique are those on freeze-drying of viruses, roller-tube tissue cultures, and certain aspects of bright- and dark-field microscopy. There is a particularly valuable section by Dr. Hallauer on the haemagglutination phenomenon; this development has revolutionized virus research since the publication of the original volumes of the *Handbuch*, and it is difficult to find elsewhere detailed reviews of the enormous literature which has accumulated on the subject. There is a short article on variation in influenza viruses by Sir Macfarlane Burnet, and an interesting analysis by Dr. Monroe Eaton of virus pneumonias. The book is superbly printed and illustrated; there are complete bibliographies; and, although the price is high, no medical reference laboratory can afford to lack a copy.

Dr. Kidd has edited a book of quite another type. Again the volume is a composite one, the work of many authors; again those chosen to discuss the various topics can speak as authorities in their field. But the aim has been to present short and stimulating reviews with carefully selected bibliographies which shall acquaint microbiologists and allied laboratory and clinical investigators with the facts about a particular specialized field. In consequence most of the fifteen articles make easy reading and they tend to represent personal points of view. There is one article in particular which should especially delight all epidemiologists—Dr. Richard Shope's study of the origin of the virus responsible for infecting the first cases in an outbreak. Dr. Frank Fenner has very succinctly reviewed his own work on mousepox, and this should interest many clinicians and epidemiologists because of the analogies with variola. There is a short article by Dr. Wyckoff on the electron-microscopic study of virus growth and a stimulating study by Dr. Kidd of proliferative lesions caused by viruses. The book is beautifully printed and illustrated and would be cheap if the dollar were at its old value.

In the third book Dr. Kenneth Smith has attempted to write an introduction to viruses which will survey the whole field, including the animal viruses, the plant viruses, and the bacterial viruses. As is well known, Dr. Smith is himself a plant virologist, and, although he has certainly mentioned the other groups, the work is so heavily weighted by his own particular interest that the book cannot be recommended as a balanced survey. It may be that to attempt such a survey at this time is to attempt the impossible. It is by no means certain that the three groups belong to a single series in the natural order, and bacterial viruses in particular are difficult to relate to the other groups at this elementary level.

FORREST FULTON.

MALARIA IN THE NEAR EAST

Anopheles and Malaria in the Near East. Anopheline Surveys in Syria and Lebanon, by H. S. Leeson, F.R.E.S., Major, R.A.M.C. Anophelism and Malaria in Transjordan and in the Neighbouring Parts of Palestine and Syria, by W. H. R. Lumsden, B.Sc., M.B., Ch.B., D.T.M.&H., Lieutenant-Colonel, R.A.M.C., and J. Yofe, M.D., D.T.M., Lieutenant-Colonel, R.A.M.C. The Anopheline Mosquitoes of Iraq and North Persia, by T. T. Macan, M.A., Ph.D., F.R.E.S., Major, R.A.M.C. Introduction by Professor P. A. Buxton, C.M.G., F.R.S. London School of Hygiene and Tropical Medicine, Memoir 7. (Pp. 223; 73 illustrations. £1 15s.) London: H. K. Lewis. 1950.

An entirely new feature in military technique was the thoroughness with which in the last war measures against malaria were intensively carried out and the success of such a policy in enabling troops even in highly malarious tropical countries to operate with remarkable freedom from effects of this disease. Though drug prophylaxis was largely responsible, this was by no means the only action taken, and one of the most important measures was the investigation of conditions relative to malaria in each area by trained malaria units and the carrying out of such measures as were indicated by these units. Incidentally in the course of their work these often amassed new knowledge about malaria in countries where little was previously known.

An outstanding example may be seen in this memoir of the London School of Hygiene on anopheles and malaria in a geographical area which includes Transjordania, Syria, Iraq, and Iran—an area which has long been of unusual zoological and medical interest. Major H. S. Leeson discusses anopheles surveys in Syria and Lebanon, Lieutenant-Colonel W. H. R. Lumsden and Lieutenant-Colonel J. Yofe discuss anopheles and malaria in Transjordania and in the neighbouring parts of Palestine and Syria, and Major T. T. Macan the anopheline mosquitoes of Iraq and North Persia. All are thorough treatises on their respective

areas and form important contributions to medical entomology. Apart from their medical and geographical interest the papers constitute the latest revision of the species of anopheles of these countries, and as such are important standard works of reference. Maps and some excellent photographs of types of country encountered accompany the papers. As noted in an introduction by Professor P. A. Buxton, the memoir is the first of the resumed publication of the series.

S. R. CHRISTOPHERS.

PSYCHO-ANALYTIC THERAPY

Technique of Psychoanalytic Therapy. By Sandor Lorand, M.D. (Pp. 251. 12s. 6d.) London: George Allen and Unwin. 1951.

Students of medical psychology, glancing through the extensive literature of psycho-analysis, often comment on the paucity of books dealing with the actual technique of the process. This is only partly explained by the difficulty of teaching a technique of psychic relations by means of the written word. Even a dictaphone cannot convey the significance of a short pause in association; and such phenomena as "resistance" can often be felt better than they can be explained, much less described. At any rate it is a fact that no systematic textbook on the subject has yet appeared. The most successful approximations have taken the form of sets of lectures to psycho-analytical students. Among these the course given over a number of years at the New York Psychoanalytical Institute by Sandor Lorand, a teacher of ripe experience, is now presented in book form and stands deservedly high as a practical introduction to analytical technique.

Of the many ways of approaching the subject the author has chosen to follow the method of outlining the course of analysis in different psychopathological states, citing illustrative cases from among the hysterias, obsessional neuroses, sexual disorders, character difficulties, and depressions. To this end he has had perforce to sacrifice any detailed account of the theoretical basis of analytical therapy; and his technical aphorisms are scattered throughout the work. This deficiency is to some extent compensated by chapters on interpretation and counter-transference respectively; the latter is a model of realism and common sense.

This is essentially a book for the use of students of psycho-analysis, though it can be read with profit by practising psychiatrists, who should not, however, expect more from the author than he sets out to give—namely, a practical outline of technique.

EDWARD GLOVER.

THE CEREBELLUM

Problems in Cerebellar Physiology. By G. Moruzzi, M.D. (Pp. 116. £1 3s. 6d.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1951.

This book consists of four lectures delivered by Professor Moruzzi at the Northwestern University Medical School in December, 1948. He discusses only limited aspects of cerebellar physiology, paying attention chiefly to the anterior lobe, which may be considered as the spinal "story" of the cerebellum. Some fifty years ago Sherrington found that decerebrate rigidity could be inhibited by faradization of the anterior vermis of the cerebellum, and, though comparatively little importance was attached to this finding at the time, Moruzzi considers that it was as fundamental for cerebellar physiology as Fritsch and Hitzig's celebrated stimulation experiments were for the physiology of the cerebral cortex.

The first two lectures are devoted to a study of experimental work done in his own department and in America as an outcome of this classical experiment, and Moruzzi concludes that the anterior lobe of the cerebellum has many features in common with the cortical suppressor areas, since they both inhibit spinal motor neurones through reticulospinal paths. In the third lecture he analyses the physiological connexions between the anterior cerebellar lobe and the cerebral cortex, and in the fourth gives an interesting account of experimental work on the possible relationship between this lobe of the cerebellum and the control of autonomic activity. Though the results are still inconclusive they indicate the need for further work on this largely unexplored aspect of cerebellar physiology, and, as Moruzzi remarks, Thomas Willis three centuries ago attempted to localize in the cerebellum the central control of the viscera. This monograph will be valuable to everyone interested in neurophysiology.

J. W. ALDREN TURNER.

SEX VARIANTS

Sex Variants. A Study of Homosexual Patterns. By George W. Henry, M.D. With Sections contributed by Specialists in Particular Fields. Sponsored by the Committee for the Study of Sex Variants, Inc. (Pp. 1,130; 31 figures. £2 2s.) London: Cassell and Co. 1950.

We are told that this book was sponsored by the Committee for the Study of Sex Variants, which was founded in 1935. It is certainly a strange book. Its arrangement is as follows: Part 1 deals with men; and they are considered under three main headings—bisexual cases, homosexual cases, narcissistic cases. Part 2, which deals with women, is arranged in the same way. I did my best, but failed signally, to discover any real differences between the three categories. Nearly all the homosexuals, so-called, as well as the bisexuals [*sic*] appear to have enjoyed both homosexual and heterosexual outlets; and few of the alleged narcissists were outstandingly narcissistic.

Each case was presented in the following way: (1) general impression, by the author; (2) family background, by the author; (3) personal history, by the subject; (4) physical examination, by the author; (5) *x*-ray examination, by a specialist; (6) comment, by the author; (7) résumé, by the author. In almost every case the personal history is of interest and value, not so much, perhaps, from the psychiatric point of view as for the light that it throws on the social background of the North American continent. The physical examinations and the *x*-ray investigations are quite valueless, for they appear to have been conducted haphazard and without set purpose. The author's commentaries are likewise superficial and perfunctory.

The Kinsey report was important in that it broke down the information that it collected and presented it statistically; and the report covered the whole field of sexual activity in the human male. It seems a pity that a much more circumscribed study, such as the one under review, should not have been conducted on lines which would have brought out the facts more forcibly. After reading this book, I feel that I know

very little more about psychosexual variants than I did before, although a great deal more about the social setting against which these human dramas were enacted; but I believe that an imaginative novelist could have done the job better. One day, it is to be hoped, a devoted team of psychiatrists, sociologists, biochemists, anthropologists, and statisticians, led by a man of originality and wide human sympathies, will study the problem of the sexual deviant creatively, but the time is evidently not yet.

E. B. STRAUSS.

TREATISE ON OPHTHALMOLOGY

Manuel d'Ophtalmologie. By P. Bailliart and A. Magitot. (Pp. 1,168; 602 figures.) Paris: G. Doin et Cie and Masson et Cie. 1950.

This textbook is intended, according to the authors, for students and the newly qualified who desire to gain the first ideas about ophthalmology. It can only be said that they have treated their intended public liberally. They plead that, although 30 years ago a volume of 300 pages would have sufficed, scientific progress has been such as to demand a treatise four times that size.

The book gives the impression of careful and studied preparation, as one would expect. There are four main divisions headed respectively generalities, affections of the globe and adnexa, surgical technique, and refraction; an appendix deals briefly with industrial, social, and Service ophthalmological matters; there is an excellent alphabetical index, and an analytical table of contents. Methods and technique of examination are well described. The volume does not include separate sections upon anatomy and physiology. The diagrams and drawings are good; some of the photographic reproductions are not so happy. There are no coloured plates. This is an up-to-date textbook of ophthalmology which will be most useful.

FRANK W. LAW.

CLEFT PALATE

Cleft Palate and Speech. By Muriel E. Morley, B.Sc., F.C.S.T. Second edition. Foreword by Professor T. P. Kilner, C.B.E., F.R.C.S. (Pp. 160; 56 figures. 12s. 6d.) Edinburgh: E. and S. Livingstone. 1951.

This useful book begins with an account of the mechanism by which the nasopharynx is closed. If it be objected that this is a matter which should be left to surgeons, anatomists, and physiologists, the author might reply that, until an intelligible and agreed account of this important and elementary subject is given in medical education, she has had to do the best she can to work it out for herself. Then she describes the various surgical attacks on the problem, indicating the welcome improvement from the original attitude that it was merely a question of closing a gap to the gradual realization that what was needed was the production of a function—that of voluntarily shutting the nasopharynx. The progressive improvement in function so gained has much lightened the task of speech therapists.

Miss Morley's balanced and intelligent attitude to her work is shown by her awareness that the best results of her surgical colleagues do not need her help at all, that an intelligent child who has been given a working palate before bad habits of speech have been acquired is often best left alone. She discusses the indications for speech therapy and the time at which it should be begun, and gives a full account of the processes of speech education. There is a statement of the many different obstacles to perfect enunciation, illustrated by some interesting case histories. An apparently normal child, who has been given an efficient nasopharyngeal sphincter, may persist in almost unintelligible speech. Miss Morley shows how this may be due to the lack of power of hearing speech properly, just as other children may have great difficulty in spelling owing to being unable to see written words properly. One small criticism is this: the author might point out that, just as there is a price to be paid in pain and danger for any operation, so there is a price to be paid for speech therapy in the mental strain it puts on the child and its liability to result in grimacing. The dangers of this kind are, however, much diminished by an approach as sensible and intelligent as Miss Morley's.

DENIS BROWNE.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received

Evaluation of Industrial Disability. By the Committee for Standardization of Joint Measurements in Industrial Injury Cases of the California Medical Association and Industrial Accident Commission. (Pp. 89. 32s.) London: Geoffrey Cumberlege. 1950.

Aids to Clinical Pathology. By D. Haler, M.B., B.S., D.C.P. 2nd ed. (Pp. 398. 8s. 6d.) London: Baillière, Tindall and Cox. 1951.

Contraceptive Technique. By H. Wright, M.B., B.S. (Pp. 68. 6s.) London: J. and A. Churchill. 1951.

Plastic Surgery. By C. R. McLaughlin, M.B., Ch.B., B.Chir., F.R.C.S.Ed. (Pp. 125. 12s. 6d.) London: Faber and Faber. 1951.

Genetics and the Races of Man. By W. C. Boyd, Ph.D. (Pp. 453. 30s.) Oxford: Blackwell Scientific Publications. 1950.

Health Visiting. By M. McEwan, M.B.E., S.R.N., S.C.M. (Pp. 383. 18s.) London: Faber and Faber. 1951.

Micro-Arteriography and Other Radiological Techniques Employed in Biological Research. By A. E. Barclay, O.B.E., M.D., D.Sc., F.R.C.P., F.F.R. (Pp. 102. 30s.) Oxford: Blackwell Scientific Publications. 1951.

The Day Hospital. By J. Bierer, M.D., D.Econ. (Pp. 56. 6s.) London: H. K. Lewis. 1951.

Selected Writings of Sir William Osler. Edited by a Committee of the Osler Club of London. (Pp. 278. 15s.) London: Geoffrey Cumberlege. 1951.

Anatomy of the Nervous System. By O. Larsell, M.A., Ph.D., Sc.D. 2nd ed. (Pp. 520. $9.) New York: Appleton-Century-Crofts. 1951.

Primer on Fractures. Prepared by the Special Exhibit Committee on Fractures in Co-operation with the Committee on Scientific Exhibit of the American Medical Association. 6th ed. (Pp. 109. $2.) New York: Paul B. Hoeber. 1951.

Die Liebesfähigkeit. By Dr. E. Speer. (Pp. 181. No price.) Munchen: J. F. Lehmanns. 1951.

Clinical and Prognostic Aspects of Acute Coronary Occlusion. By S. Eckerström. (Pp. 107. No price.) Göteborg: Elanders Boktryckeri Aktiebolag. 1951.

Enterobacteriaceae. By F. Kauffmann, M.D. (Pp. 338. Sch. 50.) Copenhagen: Ejnar Munksgaard. 1951.

Der Dünndarm im Röntgenbild. By Professor F. Kuhlmann. (Pp. 110. M. 11.80.) Berlin: Urban and Schwarzenberg. 1951.

Les Otomastoidites du Nourrisson. By Dr. H. Plisnier. (Pp. 84. 420 francs.) Paris: Masson. 1950.

BRITISH MEDICAL JOURNAL

LONDON

SATURDAY MAY 19 1951

RESEARCH IN PAEDIATRICS

The whole paediatric world will be indebted to the members of the Harben Trust for their foresight in ensuring that a first-hand account of the numerous investigations carried out under the inspiration and direction of the late Sir Leonard Parsons has a permanent place in medical literature. There have been many famous Harben lecturers, who are chosen to discuss "some subject embodying the results of original research, in conjunction with the science of public health"; among the earlier names are those of Ronald Ross, Thomas Oliver, Metchnikoff, and Ehrlich. The Trust's invitation to the late Sir Leonard Parsons to be lecturer for 1950 brought him much satisfaction and pleasure, but, characteristically, some personal anxiety lest his contribution should prove unworthy of the established high standard. His lectures[1] were delivered within one week of his lamented death, and are a modest record of his own endeavours and achievements in paediatric research and a fine tribute to the work of his colleagues and assistants at Birmingham. But the lectures go beyond a factual record of the researches conducted in Birmingham; they present Sir Leonard's carefully reasoned opinions upon many different paediatric problems. Indeed, even his friends who knew him well, and were aware of his enthusiasm and remarkable capacity for hard work, are likely to be surprised when they read these lectures and realize how varied were his paediatric interests and how brilliantly he illuminated the problems that he attacked. When, in 1920, he took charge of a ward in the Birmingham Children's Hospital no laboratory facilities for research work were available; a certain amount of morbid anatomy was done by one of the assistant physicians, but there was no biochemist, no clinical pathologist, and no adequate *x*-ray service. These conditions were, in fact, the rule in almost every children's hospital in the land at that time, and Parsons made up his mind to put Birmingham "on the map," in the sense that clinical observation and morbid anatomy were to be backed up by adequate laboratory assistance: and to unremitting labour he added not only the highest qualities of personal character but also the ability to attract, to interest, to excite, and to encourage his numerous assistants.

The three Harben Lectures do not follow the chronological order of Parsons's researches. The first is mainly an account of antenatal paediatrics, a subject that enthralled him, especially during the last 10 years of his life; and it is not until the later part of the second lecture that he mentions his earliest work on wasting disorders in young children, when he rendered a great service to paediatrics by bringing common sense and breadth of outlook to bear upon a very confused subject. Then followed the period when infantile rickets, coeliac disease, and coeliac and renal rickets were the main subjects of his researches, and these are described in the last lecture. The splendid contributions that Parsons and his team made in studying various anaemic states in infancy are discussed in the second lecture. This work, and particularly his investigation of haemolytic disease of the newborn, was done mainly between the two wars and is perhaps the high-water mark of Parsons's research activities, not only for the light that it shone upon this particular problem but for the example it set to clinical research workers of the future. Indeed, every page of the Harben Lectures bears the impress of the author's intellectual integrity, of his loyalty to his assistants, and of his own modesty, which is well exemplified by his omitting to mention that the infants' block at the Birmingham Children's Hospital, which he describes when discussing the control of infections in infancy, was dedicated to him and bears his name.

To-day, in these Harben Lectures, we read the stirring record of a life devoted to the use of biochemistry, pathology, bacteriology, and haematology as interpreters of clinical paediatrics; 50 years hence, if the lecturer is a paediatrician, what story will he have to tell? Perhaps the present-day fashion among paediatricians of paying particular attention to the mysteries of intrauterine life offers some clue. This emphasis upon the importance of antenatal paediatrics has grown as a natural counterpart to other developments: the advances of biochemistry and their application by experimental embryologists, the discovery that in certain animals deformities may be caused by vitamin deficiencies in the mothers' diets and by other influences operating upon the mother early in pregnancy, and the observation that German measles may, in the human subject, be one such harmful influence are but a few of the factors that have played some part. The effect has been to underline the fundamental significance of growth and development as the outstanding characteristics of

[1] *J. R. Inst. publ. Hlth*, 1951, **14**, 83, 95, and 124.

child life and to focus attention upon the sensitivity of immature creatures to environmental conditions. If health is to be preserved, the first essential must be that growth and development shall be able to proceed normally, and this applies not only to antenatal life but throughout the whole of childhood.

A few weeks before his death Sir Leonard Parsons gave an impressive address at the opening of the Department of Child Health of the Welsh National School of Medicine. In this (see page 1137) he discussed among other things the growth of preventive paediatrics. Up to the present there has been a somewhat artificial separation of preventive from curative paediatrics, and, though the two camps are drawing together, real vitality will not be generated until there is complete union. There is a need for fuller study of normal childhood by appropriately trained and intelligent workers, and to this end there must be enlargement of the university departments and institutes of child health to include such workers. Alternatively, research work of this type must be encouraged in other university departments—for instance, in those concerned with physiology and psychology. There will, of course, be continuing opportunity for advances in clinical paediatrics and for direct personal service to the patient—work which gives the satisfaction described by Florence Nightingale in these words: "If I have anything of the kind to do I can do without marriage or intellect or social intercourse or any of the things people sigh after. . . . I want nothing else, my heart is filled." Clinicians, if they so desire, can usefully give a "prophylactic" flavour to their work by emphasis upon those types of physical disorder that are at present mainly responsible for ill-health in childhood—trauma, respiratory infections, the common infectious fevers, and, in infancy, disorders of nutrition. There are also great opportunities for linking prevention and treatment more closely in the field of mental ill-health. But the trend of progress in paediatrics is likely to put the healthy child rather than the sick child in the centre of the picture, and the successive gradations down the scale of full health, average health, subnormal health, and disease will be studied in that order. This reversal of the present-day pattern—so fruitfully followed by Parsons—in which disease is traced back to its sources, is no novel conception but rather a question of viewpoint and emphasis. One desirable result will be to remove any artificial division that at present exists in the paediatric structure. To enlarge our knowledge and understanding of health, especially during the period of most active growth and development, is becoming increasingly important in the interests both of the individual and of the nation.

PNEUMOCONIOSIS IN SOUTH WALES

Between 1931 and 1948 more than 22,000 British coal-miners had to leave their work because they were suffering from pneumoconiosis. Nineteen thousand of these men were from South Wales, where the incidence of this disease is 40 times as great as in the rest of Britain. This concentration of disabled men in one coalfield has given rise to a very serious social problem, recently reviewed by Hugh-Jones and Fletcher.[1] Approximately 10% of an estimated population of 43,000 certified and uncertified cases of pneumoconiosis are unemployed yet capable of work under normal industrial conditions. No country can view without serious concern a situation in which men disabled by serving a vital industry cannot find work at a time when there are more jobs than men to fill them. Nor can it afford to allow younger men to be discouraged from mining by seeing groups of unemployed disabled miners at the street corners of mining villages.

Well-intended welfare schemes—such as the Disabled Persons (Employment) Act, the Grenfell and Remploy Factories, and the encouragement given by the Board of Trade to private industry to come into South Wales—have not met the needs of these men. The physical disability of breathlessness among the more disabled prevents them from doing heavy unskilled work, which is plentiful in South Wales. Most of them have reached the age of 50 and feel incapable of learning new skills for light work or of competing against the younger men and womenfolk for the light unskilled jobs. Moreover, they are crowded together in the Welsh valleys, where there is no alternative to mining and where transport to other areas is difficult. To make matters worse, they live in a region where 11% of the male working population is disabled. Thus competition for the few jobs they can do is high, and to register as a disabled person is of no help. Some men refuse to take this step, because they consider they have better prospects of finding work in the normal labour market. It is easy to understand their reluctance to break their ties with Wales to find jobs in other regions. Hugh-Jones and Fletcher suggest that a system of medical follow-up and grading of ex-miners with pneumoconiosis would give them the reassurance that so many of them need and could steer them into appropriate jobs. Writing as doctors, they do not consider it within their province to make any social or economic recommendations. This is the concern of various Government Departments. Since 1947 a National Joint Pneumoconiosis Committee

[1] *Social Consequences of Pneumoconiosis among Coalminers in South Wales* (Medical Research Council Memorandum No. 25), 1951, H.M.S.O., London.
[2] *Brit. J. industr. Med.*, 1951, **8**, 53.

has co-ordinated the activities of these departments. Through one of its subcommittees it has considered the problem of re-employment, and the Ministry of Labour and the Board of Trade have acted energetically on the advice given by this committee. It would be interesting to know more about the measures that have been taken to deal with the problem and why they have not been successful.

Although the Pneumoconiosis Research Unit has not given an answer to the immediate problem of finding work for these men, in this and its other publications it is evident that it has already made a contribution which will bring great benefits to the mining community. There is now enough evidence to show that pneumoconiosis consists of two disease processes: the first, simple pneumoconiosis, due to the action of dusts alone; and the second, progressive massive fibrosis, which occurs only in well-established simple cases from a superimposed infection. Men with the earlier stages of simple pneumoconiosis are now allowed to continue work in mines, if they so wish, under medical supervision. This ends the unnecessary suspension of many reasonably fit miners with the simple form of disease; some of these bitterly resented the regulations of the Workmen's Compensation Act which took their jobs away from them.

The prevention of this disease depends ultimately on dust suppression, which in a coal mine is very costly. Complete suppression of dust is impracticable, and information wanted by engineers is the concentration of airborne dust which is low enough not to give rise to pneumoconiosis. In another report[2] Fletcher and his colleagues claim that the introduction of periodic radiological examinations of coal-miners in conjunction with routine dust estimations would in time indicate safe standards of dustiness. Before these have been defined the periodic examinations would reveal the pits where early signs of the disease were arising and enable the engineers to concentrate on them. Disability develops late in coal-workers' pneumoconiosis, but radiological changes, indicating a danger of later disability, usually appear before irreparable damage has been done to the lungs. Such a scheme would give immediate protection to the men still in the mines. It could also be combined with the suggested supervision and replacement of disabled ex-miners. This might help to solve the immediate problem of unemployment, by giving the men who are fit enough to do mining, and want to do it, the opportunity to return to the work which was unnecessarily taken away from them by well-intended but misguided regulations.

ELECTROCARDIOGRAPHIC DIAGNOSIS OF ANGINA

The diagnosis of angina pectoris depends almost entirely upon careful assessment of subjective sensations described by the patient, since definite physical signs of heart disease are seldom found. As in other disorders in which reliance must be placed on symptoms alone, difficulties arise when the symptoms are atypical or when the history is confused by functional disturbances unrelated to the disease. In such cases a reliable objective test would be invaluable, and many attempts have been made to evolve an electrocardiographic test for the diagnosis of angina. Although the electrocardiogram is usually normal in patients with angina, it has been known for many years that definite changes can be demonstrated if the tracing is taken during an attack.[1] Hence it appeared likely that induced myocardial anoxia might be used as a test in anginal subjects to bring about similar cardiographic changes. Tests entailing the breathing of air with a low percentage of oxygen have been described,[2] but the technical difficulties and the potential risk to life have precluded their general use. Electrocardiographic examination after sustained exertion has proved a more simple and reliable procedure, and the "2-step" exercise test of Master has hitherto been regarded as being the most satisfactory of such tests.[3 4] In this patients are examined electrocardiographically before and after taking a standard amount of exercise according to age, weight, and sex. Depression of the RS–T segment below the iso-electric level or a change from a normal to a flat, biphasic, or inverted T wave are found in patients with coronary insufficiency. The number of positive results obtained with this test has varied with the criteria adopted for RS–T depression by different observers, but it is probable that it is of diagnostic value in about 50% of patients with angina.

Recently Paul Wood and his colleagues[5] have described a simplified test which promises to be more reliable than that of Master. In this modified effort test a control electrocardiogram, including standard leads, unipolar limb leads, and unipolar chest leads (V_{1-6}), is taken at rest and repeated at half-minute intervals after the patient has been exercised until pain, dyspnoea, or fatigue has called a halt. The use of a direct recording electrocardiograph greatly facilitates the interpretation of the tracings, since it is possible to detect at a glance the lead in which the changes are most marked. To assess the value of their test Wood and his co-workers carried out a comparative investigation on 100 patients with angina pectoris but without abnormalities in the resting electrocardiogram and on the same number of healthy subjects. It was found that in some healthy individuals after exercise there was a depression of the RS–T junction followed by an RS–T segment which rose sharply to a normal T wave. Slight flat depression of the RS–T segment, not more than 0.5 mm.

[1] Bousfield, G., *Lancet*, 1918, **2**, 457.
[2] Levy, R. L., Patterson, J. E., Clerk, T. W., and Bruenn, H. G., *J. Amer. med. Ass.*, 1941, **117**, 2113.
[3] Master, A. M., *Amer. Heart J.*, 1935, **10**, 495.
[4] —— *Ann. intern. Med.*, 1950, **32**, 842.
[5] *Brit. Heart J.*, 1950, **12**, 363.

below the P–Q level, was found in a few of the controls. Of the patients with angina pectoris, 88% developed characteristic changes in the left ventricular leads, lead V_5 being most commonly altered. The usual changes consisted of a flat or sagging depression, greater than 1 mm., of the RS–T segment; less commonly the T wave was flat, biphasic, or inverted. Transient bundle branch block was seen in two cases. The proportion of positive results was far higher than that obtained by any previous effort test, a fact probably due to the alteration of the criteria for limiting the amount of effort. Indeed, it seems fundamentally wrong that a standardized effort test should be applied to a disease like angina pectoris in which the factors precipitating an attack are so variable. Other reasons for the success of this test are the routine use of the direct-recording electrocardiograph and the clear distinction between depression of the RS–T junction and definite flat or sagging depression of the RS–T segment.

THE MOSQUITO AND ITS PREY

There is a popular idea that mosquitoes prefer to bite certain individuals. The evidence from subsequent skin eruptions, however, is unreliable, for people equally bitten may exhibit all degrees of skin reaction from severe to none at all. Nevertheless, there is some sound support for the idea. Certain African mosquitoes have been consistently observed to attack some men in preference to others, though an individual's attractiveness varied from time to time.[1] It has also been found that biting mosquitoes prefer full huts, containing sleeping Africans, rather than empty ones; and more are attracted by numerous and unwashed sleepers than by few or washed ones.[2] Thorough cleansing with soap and water decreases attractiveness.[3] Artificial tests suggest that they can be attracted by such crude stimuli as warm objects,[4] lights at night,[5] dark objects by day,[6] and the gas carbon dioxide,[5] though there is controversy about this last, and some authors[7] deny its effect. The unreliability of simple stimuli is not surprising. Instinctive behaviour reacts to a pattern of impressions rather than to a single sensation; thus a mosquito may well behave erratically in response to warmth or CO_2 divorced from the shape and humidity associated with a real man or animal, and the African field observations suggest that mosquitoes possess considerable discernment. Recent tests[6] in the open in Ontario and Labrador attempted to avoid this difficulty. Robots dressed in human clothing, kept warm by hot water inside, and exhaling gases through a "mouth-hole," were set up as targets for the viciously biting species of *Aëdes* which infest those regions. Under these conditions dark clothing was found to be more attractive than light, rough than smooth; and damp than dry in warm weather, though the reverse was true in the cold. Carbon dioxide blown from the "mouth" increased the robot's attractiveness, and so, strangely enough, did the vapours of ether and petrol. This is largely in line with much earlier work summarized by Marston Bates.[8]

But experimental work of this kind, aimed at devising better mosquito repellents, must in the end be related always to the natural behaviour of the mosquito towards man, and unfortunately field observations have hitherto been all too few. Dr. R. C. Muirhead-Thomson's work reported on page 1114 of this issue has therefore a double importance when it reveals that adults are preferred to children, and men to women, at least by Jamaican mosquitoes. It shows which members of the population particularly require protection, and suggests that there may be some sexual factor in attractiveness. It also—and this is equally important—throws a completely new light on the epidemiology of malaria. If children under 2 are very rarely bitten, their noted freedom from the symptoms of malaria may simply be due to this fact rather than to a malarial immunity. And if mosquitoes pay them little attention they can hardly be the natural reservoir of the malarial parasite and responsible for infecting harmless mosquitoes. This West Indian work is promising and demands to be extended by field observations on a wide front. Though the habits of *Anopheles albimanus* in Central America and the Greater Antilles may make observation fairly easy, the difficulties in Africa and Europe are not insuperable, and attempts should now be made to eliminate this gap in our knowledge of mosquito natural history.

1 Ribbands, C. R., *Nature, Lond.*, 1946, **158**, 912.
2 Haddow, A. J., *Bull. ent. Res.*, 1942, **33**, 91.
3 De Meillon, B., *Publ. S. Afr. Inst. med. Res.*, 1935, **6**, 323.
4 Crumb, S. E., *Science*, 1922, **55**, 446.
5 Huffaker, C. B., and Back, R. C., *J. econ. Ent.*, 1943, **36**, 561.
6 Brown, A. W. A., *Nature, Lond.*, 1951, **167**, 202.
7 Dethier, V. G., *Chemical Insect Attractants and Repellents*, 1947, Toronto.
8 *The Natural History of Mosquitoes*, 1949, pp 66–76, New York.

STUDENTS FEEL THE STRAIN

Last autumn, at the beginning of the academic year, there were 83,592 university students in England, Wales, and Scotland,[1] almost exactly in the proportion of three men to one woman,[2] and as a rough estimate it may be taken that one man in twenty and one woman in sixty is selected for university education. The quick establishment of health services in almost all British universities during the last few years has brought some interesting facts to light about this highly selected group of people. The medical officers in charge of these services quite rightly paid immediate attention to tuberculosis, because it is a recognized danger to young adult life and because of its ability to produce local epidemics in partially closed communities. At student health conferences, however, it was soon apparent that mental ill-health was likely to rival tuberculosis as a serious handicap to normal undergraduate life, and nearly two years ago a committee was convened to consider the causes of mental ill-health among students. A system of notification of numbers (not names) of cases of serious mental breakdown during the present academic year has been organized which will, with sufficient co-operation, provide a comprehensive picture for the country as a whole. As forerunners of more exact knowledge in this field two recent reports may be cited

1 *The Economist*, March 24, 1951.
2 *The Problem Facing British Universities*, 1948, London, p. 108.
3 Report to the University of Wales on the Student Health Service for 1949–50 Session.
4 *Lancet*, 1951, **1**, 731.

—one by Hitchens, Grant, and McKnight[3] (from the University of Wales) and the other by Parnell[4] (from Oxford). In each report, largely through the co-operation of college authorities and university registrars, figures are presented which demonstrate clearly the relative importance of mental illness and tuberculosis. From Wales, with a university population this year numbering 5,124, it is reported that 37 students (from all academic years) failed to complete last year's session through mental ill-health. At Oxford it was found in a survey of prolonged illness causing not less than a term's absence that mental illness and nervous breakdown accounted for 52.5% of the whole, tuberculosis for 23%, and other conditions for 24%. As an indication of more serious disturbance 9 of the 35 undergraduate deaths in the three years 1947–9 were suicidal. If these figures are typical of what may be found in other universities, there seems to be an urgent need to examine the relative importance of the various causes of mental ill-health in students—causes which include such stresses as those due to academic difficulty, examinations, trouble at home, fear of disease, problems associated with sex, and with mental staleness or fatigue. Financial difficulties, because an increasing number of students receive grants, are probably less frequent than they once were, though the fear of failure and consequent loss of grant may be intense. Few serious students, of course, would claim that they had never felt the effect of mental strain. At this time of the year, in the weeks preceding examinations, health officers have learnt to expect a crop of complaints, especially insomnia. The remedy is obscure. No known psychological tests and no assessment of work by supervisors can exactly replace the standardized test of performance in examinations, though change in the examination time-table might lessen the strain. And to require a bill of psychological health before admission to a university might exclude many first-class students.

ANTIBIOTICS FROM LICHENS

During the past 10 years the entire vegetable kingdom has been ransacked in the search for new antibiotics, and among the quainter plants in which this search has yielded some results are the lichens. In any such exploration an interesting possibility always to be borne in mind is that an explanation may be found for the action of some ancient remedy, whether in folk-lore or pharmacopoeia. Lichens are particularly promising in this connexion, since their medicinal use goes back beyond the time of Hippocrates, and they have been employed in many countries for a variety of purposes, some of which, such as the treatment of coughs generally, or phthisis, and application to wounds or inflamed areas, are consistent with antibiotic activity. K. O. Vartia[1] prefaces an account of his own work on this subject with a review of these earlier uses. Many of these are merely magical or superstitious—for example, "Mucus cranii humani," lichen grown on a human skull, was "worth its weight in gold." Nevertheless, some of them may have had a genuine effect: lichen extracts have been official remedies and the subject of pharmacological study. Several of the acids which are their active constituents were identified years ago and their other properties determined before the present place of antibiotics in medicine was even imagined.

The study of these substances as antibiotics has been pursued only during the past five years, and has centred largly on usnic acid, which has a considerable degree of activity not only against various Gram-positive species of bacteria but also against the tubercle bacillus. It emerges as generally the most active substance from the extensive survey now reported by Vartia. He began by testing 149 varieties of lichen collected in Finland against eight species of bacteria, by placing a fragment of the plant on an inoculated plate: 75 inhibited the growth of some species, and in most, but not all, this was the effect of a known constituent. Further tests were done by a more elaborate quantitative method with purified extracts of known chemical composition, to determine the degree of activity against a considerable range of ordinary bacteria, tubercle bacilli, and certain fungi. The results furnish a comprehensive picture of the antimicrobic activity of these interesting compounds. Only one has any effect on Gram-negative species of bacteria: Gram-positive species are the most highly and frequently susceptible, activity against tubercle bacilli being less frequent and generally of a lower order (although this fact, as the author points out, may have been due in part to the size of his inoculum), and that against fungi still less marked. Vartia believes that there is still scope for further work in this field, and even seems to entertain the possibility that usnic acid may prove useful as an adjuvant to streptomycin in the treatment of tuberculosis.

[1] *Ann. Med. exp. Biol. fenn.*, 1950, Suppl. 7.

OLD AND YOUNG

To live to 100 years is an unusual achievement, but more people than formerly are attaining that distinction. According to the Registrar-General,[1] 116 people reputedly aged 100 or over died in England and Wales in 1946 and the same number in 1947. The average number who did so in the six years 1940–5 was 105, and in the five years 1935–9 102. Women have a notable advantage over men here, for, of the 232 deaths of people aged 100 years or over in 1946–7, 191 were women. In each year one woman died at the age of 108. The nearest male competitor to these two was aged 106 at death in 1947.

At the other end of life the death rates continue to improve. The infant mortality rate in England and Wales was 42.9 per thousand related live births in 1946, 41.4 in 1947, and the provisional figure for 1950 was 29.8. In 1946 and 1947 the north region had the highest infant mortality rate (51.5 and 50.7), while the south-east had the lowest (34.5 and 32.7). Between 1937–9 and 1947 the greatest regional reduction in the infant mortality rate was in Greater London with a 34% decrease, while in the north region and in Wales reductions amounted

to only 19% and 18%. As the Registrar-General says, it is unsatisfactory that the two regions which have persistently had very high rates are the two that show the smallest relative reductions since 1937–9.

The neonatal and infant mortality rates in 1947 in England and Wales are compared in the following table with those of certain other countries:

Country	Neonatal Mortality Rate	Infant Mortality Rate	% N.M.R./I.M.R
England and Wales ..	22·3	41	54
Canada	25·9	45	58
Australia	20·5	29	71
New Zealand	17·7	25	71
U.S.A.	22·3	32	70

The most notable differences are in the infant mortality rate, the rates for England and Wales and for Canada being notably higher than the others. The figures in the last column emphasize the relative importance in these two countries in 1947 of deaths of children aged 1 month to 1 year. In this age group social conditions probably exert a greater influence on the death rate than they do during the first month of life.

The Registrar-General has some interesting comments to make on deaths from accidental mechanical suffocation. In 1931 there were 333 deaths certified as due to this cause. In 1939 there were 384; in 1945 there were 600, and in 1947 there were 911. A higher birth rate does not account for these increasing numbers. Whether the deaths are, in fact, due to suffocation or not is a point that has been debated, and suggestions have been made[2-5] that fulminating pneumonia is the true cause in many cases. But, as the Registrar-General points out, whatever may be the true cause of death, it is difficult to account for the increasing number of deaths *certified* as resulting from accidental mechanical suffocation.

"FREE DIET" IN DIABETES

The significance of hyperglycaemia in the human diabetic has long been the subject of controversy. It is generally agreed that hyperglycaemia is the cause of such symptoms as thirst, polyuria, and pruritus vulvae, but there is at present no conclusive evidence that it is wholly or even in part responsible for the vascular and retinal complications of the disease. Joslin and his co-workers in America and Graham and Lawrence in this country have always taken the view that the surest way to avoid such complications is to maintain the best blood-sugar control compatible with safety and a reasonably normal mode of life. Priscilla White has recently brought forward some evidence in support of the view that the incidence of vascular and retinal complications is greater in those long-standing cases of diabetes with poor blood-sugar control than in those in which it has been well maintained. The objection to this conclusion is the impossibility of estimating with any degree of accuracy how effectively the blood sugar has been controlled over a period of years. On the other hand, Dolger[1] has found that duration of diabetes is the only factor of importance and that the incidence of complications is uninfluenced by the degree of control.

In the face of such divergent opinions the report of Drs. C. C. Forsyth, T. W. G. Kinnear, and Professor D. M. Dunlop on 50 cases of diabetes treated for a period of five years on so-called "free diet" and insulin is of interest and importance to all who treat diabetes, and particularly to those in charge of diabetic clinics. The term "free diet" has been somewhat modified to mean a diet dictated by appetite except for the omission of table sugar, jam, chocolate, and sweets, though rather surprisingly it never contained less than 200 g. of carbohydrate per day. The results were very much what might be expected: clinical control—that is, freedom from hunger, thirst, pruritus, nocturia, and ketosis—was readily achieved in 39 out of the 50 cases, the remaining 11 having to be put back on a more conventional restricted diet because of frequent hypoglycaemia, excessive insulin requirement, or pruritus vulvae. The problem of obesity was avoided by confining the investigation to diabetics who showed no tendency to be fat before the onset of the disease. The insulin requirements of young patients showed the greatest rise, and the authors discuss the significance of this in relation to modern conceptions of the aetiology of diabetes.

Apart from the dangers of hypoglycaemia attendant upon the use of a truly "free" as opposed to an unrestricted diet, the only really important issue is that of the incidence of complications in patients so treated, and on this all-important point the Edinburgh investigation throws no light—in fact, it casts a little gloom. In the absence of more detailed information about the duration of diabetes it is difficult to assess the significance of the occurrence during the five-year trial period of retinitis in four of the patients having the "free diet"; the absence of any reference to complications arising in the control group presumably must be taken as indicating that there were none. If this inference is correct it is at any rate still unjustifiable to regard "free diet" as being as good as, far less better than, the adequate but controlled intake of carbohydrate which is favoured by most workers in this country. It would be quite unfair to the authors of this article not to emphasize that they are concerned only with the presentation of clinical observations, and do not themselves advocate "free diet" in the treatment of diabetes. There can be no doubt that the premature adoption of "free diets" might do great harm, and that only after an interval of 10 or more years might the harm done become apparent as an increase in the already deplorable incidence of vascular and retinal complications. It is to be hoped that the Edinburgh workers will continue their study, giving special attention to the incidence of complications. Meanwhile, until more is known on this subject, those who treat diabetes should not be deterred from continuing reasonably to strive after a physiological ideal, however unattainable it may be.

1 *Statistical Review of England and Wales*, 1946–7, Text Vol. I Medical, 1951 (H.M.S.O.).
2 Brend, W. A., *Enquiry into the Statistics of Deaths from Violence and Unnatural Causes in the United Kingdom*, London, 1915.
3 Davison, W. H., *British Medical Journal*, 1945, **2**, 251.
4 Bowden, K., *Med. J. Austral.*, 1950, **1**, 65.
5 Logan, W. P. D., *British Medical Journal*, 1951, **1**, 815.

1 *J. Amer. med. Ass.*, 1947, **134**, 1289.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

THE ACUTE MENTAL CASE

BY

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Acute mental cases can be divided into those in which the diagnosis is obvious and those in which it is not. If an individual becomes violent and noisy it is clear to all that something should be done; but when patients are quiet and do not show dramatic changes in behaviour the need for action may not be realized until it is too late. A substantial number of potentially recoverable melancholics are permitted to commit suicide because the severity of their condition is not realized.

The incidence of acute mental breakdown is high. In round figures, of the 20,000 Health Service patients admitted to mental hospitals in England and Wales in 1950, 1,000 (5%) were admitted on Urgency Orders. In addition, a high proportion of the patients not so admitted—for example, many voluntary patients—suffered from acute conditions. In 1948, 4,604 individuals (2,900 males and 1,704 females) committed suicide; there were probably ten or even twenty times that number of unsuccessful attempts. Most murders are committed by the insane; 30–40% of murderers commit suicide before arrest.

History Taking

An independent account is quite essential, as from the nature of their condition acute mental patients are usually uncooperative or even actively antagonistic. Difficulties often arise and much time is wasted because doctors are rushed off to see a patient knowing nothing except that he has become "violent." An adequate opinion about the diagnosis and appropriate treatment can seldom be formed solely from an examination of the patient without prior knowledge of the past history and the development of the symptoms. Again, the assistance and equipment that may be necessary should often be mobilized before the patient is examined, if struggles and scenes are to be avoided. It is, for example, both difficult and dangerous to give an injection to any resistant adult without assistance.

A satisfactory history can seldom be obtained from more than one informant at a time. The worst possible conditions are to have a number of agitated relations and friends all together, interrupting and contradicting each other, with perhaps "noises off" from the patient concerned, or, worse still, with the patient repeatedly trying to get into the room to see what is going on. The most sensible and informed relations and friends should be seen separately. If possible, they should be induced to come round to one's house; or an assignation can be made in a house or flat near that of the patient. If neither of these courses is practicable, the relatives can be seen in one's car. In this connexion it is difficult to write on the steering wheel and annoying to have the informant overlooking one's notes. It is better to sit in the back seat with the informant in the front seat.

The main practical issues are (*a*) whether the acute mental condition is of such a type and severity and probable duration that admission to hospital, and in particular to a mental hospital or observation ward, is called for; or (*b*) whether it is likely to be a transient reaction with a reasonable prospect of settling rapidly at home.

Broadly speaking, with the exception of the psychopathic, the hysterical, and the acute alcoholic, most patients who can reasonably be regarded as acute mental cases need hospital care as soon as possible. With few exceptions, they will need sedation and subsequent observation and supervision, at least for a time. The great thing is to have sufficient sedation and enough assistants.

Diagnostic Categories

The diagnostic categories likely to result in acute mental states may be listed as follows: (1) manic-depressive psychoses and the involutional melancholias; (2) schizophrenia; (3) organic reactions, especially toxic confusional conditions (including alcohol); and (4) hysterical and psychopathic outbursts.

It is clearly impossible to summarize briefly the possible symptoms in all these conditions. Moreover, mixtures are not infrequent—for example, hysteria and alcohol. Nevertheless, the following points may be of some value.

Manic-depressive Psychoses and Involutional Melancholias.—Manic-depressive psychoses and involutional melancholias seldom show a really acute onset, and, though not invariably, occur in relatively stable individuals, so that the breakdowns come as a surprise to the informant, unless there is a history of a previous attack. There is a history of increasing excitement or depression extending over days or weeks. Manics may be socially impossible but are seldom actively dangerous to others—that is, homicidal. The milder or "hypomanic" cases can present the most difficult problem of any, when not certifiable.

The risk in depressions is of course mainly that of suicide; the popular fallacy still persists that those who talk of suicide are unlikely to do it: nothing could be more mistaken.

Those with depressions may be difficult to diagnose because they are transiently better after an unsuccessful attempt at suicide. Good indications of severity are definite ideas of reference (the belief that others are talking about them and looking at them in a disparaging way), self-reproachful ideas of sin, the belief that the police are after them, delusions of disease—for example, venereal disease—and delusions of poverty. In my experience the commonest psychiatric mistake is not to take depressions seriously enough.

Schizophrenia.—The apparently sudden development of a state of excitement or violence is relatively common in schizophrenia. Schizophrenics can be extremely impulsive and dangerous, quite suddenly and without warning. Special care and precautions are therefore necessary. The history will usually disclose

premonitory symptoms of being abstracted and withdrawn, of decrease in activity and "remoteness," coupled with persecutory ideas. Various odd misinterpretations and the finding of "special meanings" are highly characteristic, as also is talk of being hypnotized.

Organic Reactions.—Conditions of severe and dangerous excitement can occur in general paralysis of the insane, nowadays a rare condition. The history should disclose impairment of judgment, memory, and grasp. Toxic confusional ("delirious") states are typically variable, and are characterized by restlessness and above all by confusion. Paranoid or persecutory delusional ideas, typically fluctuating in intensity, are very common. These states tend to be worse at night and there is increased restlessness then; for example, patients may try to dress up and go out. Visual hallucinations are in practice diagnostic of a toxic confusional condition. Owing to the increasing number of old people, one sees more and more delirious reactions in the aged or senile. Occasionally prolonged and dangerous confusional states occur in epileptics. With alcohol one must remember that drinking can be symptomatic of other conditions, in which case there will be a history of symptoms preceding the indulgence. Delirium tremens is now relatively rare, but I have been surprised to see a number of typical cases not recognized; the usual duration is three to five days. The possibility of drug intoxication should be borne in mind in any unexplained confusional state, and the room should be searched for evidence of this.

Hysterical and Psychopathic Outbursts.—Of this group it can be said that a past history of instability is invariable, unless there is also a history of quite exceptional stress. These reactions are therefore *not* a source of surprise to the friends or relations who have seen comparable manifestations before. This group includes the emotionally unstable people who indulge in violent outbursts when confronted with difficulties or when they cannot get their own way. These outbursts are typically histrionic, melodramatic, and uncontrolled; but the patients remain well in touch, the whole condition being highly reactive to environmental factors. Accusations, complaints, and threats may be made; but true paranoid delusional ideas are not expressed.

General Management

Acute mental patients need to be under care, supervision, and control, for their own benefit and that of society, until their acute mental breakdown has subsided. The first step must usually be to achieve adequate sedation, to be continued as necessary. When not in hospital, similar precautions should be taken, so far as is possible.

Acute mental patients will often reject control and refuse sedation. When this occurs, force must be used. As trained nurses are seldom available, untrained helpers must be used instead. The cardinal importance of having enough assistants has already been emphasized. It is far better to have too many than too few: at least three helpers should be available. Moreover, patients will often stop resisting when it is clear that this is useless. If necessary, there should be no hesitation in calling in the help of the police.

Discretion must be exercised in deciding when to use force. If a patient is actively violent he should be controlled as soon as possible; but it is often reasonable to postpone any exhibition of force until the time comes for compulsory removal to hospital. In any doubtful case this should be preceded by adequate sedation to facilitate the removal to the ambulance or car.

When confronted with a powerful patient who is armed or clearly prepared to put up a fight, it may be helpful to throw a bucket of water over him before seizing him. A low-pressure hose, if available, affords the safest and most humane method of all. Once the patient is held, first remove his boots or shoes; then his kicking is not so dangerous and it is harder for him to run away.

Sedation

The next step is to give *adequate* sedation by hypodermic injection. The syringe should be in readiness near by, but preferably out of sight; nothing is more vexing than to have one's syringe broken and no other available. It can be very difficult to remove the coat of a violently struggling patient. In such cases it may be necessary to give the injection through the clothes into the buttock while the assistants are sitting on the patient, who is on the floor face down. The needle may easily get broken off by violent muscular movement, with the unfortunate result that only the needle is injected. Needles usually snap off at the junction with the nozzle. A long—even 4-in. (10-cm.)—needle is therefore the best because it can be held distal to the nozzle so that if snapped off it is still held, and because if necessary it can be stuck *through* the clothes. The standard injection is morphine, ½ gr. (32 mg.), and hyoscine, 1/100 gr. (0.65 mg.)—¼ gr. (16 mg.) of morphine may not be enough. Other possibilities are phenobarbitone, 3 gr. (0.2 g.), or paraldehyde, usually made up in 30-min. (1.8-ml.) capsules; four of such capsules should be injected intramuscularly.

The advantage of sedation by injection is of course that a powerful action can be induced quickly. If neither of these effects are so necessary and the patient can be induced to swallow, sodium amytal, 9 gr. (0.6 g.), is useful (6 gr.—0.4 g.—is often not enough), to be repeated as necessary, but it is well to let perhaps four hours elapse. For old people chloral hydrate, 45 gr. (3 g.), repeated when necessary, is often useful; bromides are better avoided because of the risk of bromide intoxication.

Other Precautionary Measures

Undress the patient. Remove all stockings, straps, bands, and dressing-gown and pyjama cords, and anything that could possibly be used for hanging or strangulation, or swallowing—for example, handkerchiefs. Keep the patient on the ground floor, so that if he jumps out of the window he will not harm himself much. Keep him warm, perhaps with blankets on a mattress on the floor. Remove all sharp objects (scissors); lock the doors. The patient must always be accompanied to the lavatory or bathroom. Preserve a constant watch, preferably with two people; it is consoling for an untrained watcher to have another with him, and it also helps to keep him awake.

Again discretion must be used before attempting to approximate the room to a padded cell; but if mistakes are to be made it is better to make them in the direction

of unnecessary precautions. Moreover, the adoption of stringent precautions is not necessarily a bad lesson for the hysteric who may need them least.

In addition to sedation, it is very important to see that the bowels are open, for which purpose calomel (½ gr.), followed by magnesium sulphate, 2 dr. (7 ml.), the next morning, may be recommended. The fluid intake should amount to at least six pints (3.4 litres) a day. It is also important to keep the mouth washed and clean.

The Relatives

Removal to a mental hospital or observation ward still bears a considerable stigma and is apt to be strongly resented or resisted by relations. I have found the relatives of schizophrenics particularly difficult; they are often queer people themselves.

The main points to make are: (1) The patient is clearly sick and in urgent need of treatment; this can be properly carried out only in hospital. (2) An ordinary general hospital cannot admit a patient against his expressed wish, nor has it the facilities to deal with this type of case if it could. (3) All one wants to do is to achieve a period of observation; certification may not be necessary and one hopes not. (4) To convey indirectly that the main issue is what is best for the patient and not the feelings of the relations. (5) That even if certification is necessary, this is not a permanent and irrecoverable step. An astonishing number of people still believe this is so. It can also be pointed out that over 60% of the patients in mental hospitals are voluntary patients; that nobody wants to certify a patient unless it is essential; that there are the most elaborate safeguards against wrongful detention; and that, with few exceptions, patients can be removed from mental hospitals, even against medical advice, if the relations are prepared to accept responsibility.

Sometimes it is necessary to be firm and to state that unless the relations are willing to abide by the advice given it is one's medical and legal duty to inform the appropriate authorities of the position.

Admission to Hospital

If the patient or relatives are able and willing to pay the appropriate fees, the procedure for admission is by Urgency Order. The nearest friend or relation must act as petitioner. The appropriate "private" mental hospital is then rung up and the presence of a vacancy ascertained. Many are willing to send an ambulance or car with nurses. But they cannot act unless the Urgency Order is available for them to take with them. Urgency Orders may be obtained from any Law stationer.

An Urgency Order lasts for only seven days; it is not certification, and is intended to provide a breathing space pending further action. It is much the most convenient method for private patients; a magistrate need not be called in.

Do not try to write up the Urgency Order—a lengthy but self-explanatory document—except with the friend or relation who is acting as petitioner. Lead him or her off to a quiet place for the purpose, preferably near a telephone, for it will almost certainly be needed.

If not a private patient—that is, one who cannot afford private fees—the procedure nowadays is easy and consists in ringing up the duly authorized officer (formerly known as the relieving officer) of the district, and subsequently giving him or leaving for him a written report on why you think action is necessary. The D.A.O. will then make all the necessary arrangements; but they appreciate one's help. In my experience—mainly in London—they are wonderfully obliging and efficient; but quite inevitably there may be delays before they can act.

Prognosis and Treatment

It is unwise to be too dogmatic or specific or optimistic. With the exception of psychopathic or hysterical outbursts and the acute alcoholic, the duration of the illness in acute mental cases is apt to be prolonged. While it is reasonable to stress the great advances that have been made in psychiatric treatment, it is most unwise to indicate what the treatment should be. It is better to emphasize that only more prolonged investigation and observation will permit of a proper assessment of the condition, this constituting one of the main reasons for admission to hospital. To pitch hopes too high in order to get consent for action, or give your opinion on the absolute necessity for a certain type of treatment—for example, insulin shock—which may be unsuitable, is apt to cause justified bitterness and disappointment later.

Finally, to have a near friend or relation removed to a mental hospital is necessarily an extremely upsetting experience. It is therefore often reasonable and humane to give sedation to help the relation to sleep that night, sodium amytal, 3 gr., being a suitable drug for the purpose.

Conclusion

I am sure doctors are prone to act too late rather than too early. This may be in part a reflection of their lack of psychiatric knowledge and also of the reluctance of relations to take steps because of the stigma of insanity. But the "genuine" acute mental case usually needs hospital care. To repeat: the main mistakes are to have an inadequate number of helpers and to give inadequate sedation. Lastly, in self-protection, take and keep really full notes.

The air transport of casualties began during the siege of Paris in 1870, when 160 patients were successfully evacuated by balloon. The first recorded case of a casualty transported by aircraft was in 1915, when Captain Dangelza flew a wounded Serbian airman to safety during the retreat of the Serbian army. The French used air ambulances in Morocco in 1918, and the following year the R.A.F. moved patients in Somaliland. Emergency medical cases in Egypt were evacuated from isolated areas by air, and the Vickers Vimy aircraft allocated for this service bore the Geneva Red Cross. This was later removed, as it restricted the use of the aircraft, but the stretcher fittings remained so that it could be used as an ambulance when necessary. The first air ambulance service in Britain was started in 1925 at Halton, and covered a radius of 100 miles. The service was disbanded two years later, as it was found that the use of troop carriers was more economical. Between 1925 and 1938 a total of 2,112 patients were transported by the R.A.F. An air ambulance organization was established in Britain in June, 1941, consisting of seven specially fitted aircraft marked with the Red Cross and stationed at Hendon, Abbotsinch, and Wick. By V.J. Day approximately 400,000 patients had been carried by the R.A.F., and during the latter stages of the war in Europe 90% of casualties were transported by air. In the Korean war the R.A.F. are transporting British and French casualties home via the Middle East.

THE STUDY OF CHILD HEALTH*

BY

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F.R.C.O.G., F.R.S.

A great change has taken place in the standing and importance of the subject known under the various names of paediatrics, child health, and child medicine. It has advanced from being a somewhat insignificant section of medicine to become one of the major subjects of medical education; in many universities it joins medicine, surgery, and obstetrics in forming the four subjects of the final examination.

The welcome recognition of the importance of paediatrics by universities and by the General Medical Council has been the result of an educational campaign carried on for many years by the British Paediatric Association. The association gave evidence before the Goodenough Committee on Medical Schools, which in its report, published in 1944, said: "Generally in the medical schools in Great Britain the teaching about children has been inadequate and only a faint interest has been taken in the subject. The inadequacy has been due in fact to the lack of facilities for the study of the subject . . . if the place of paediatrics in the undergraduate course is to be assured, adequate recognition must be given to the subject in the final qualifying examination." Previous to the issue of this report it had often been stated by university authorities that even if academic and clinical facilities were made available for the teaching of this subject an examination would be unnecessary. I understand that the Scottish student will pursue knowledge for its own sake and without any hope of a reward. I do not know the attitude of mind of the Welsh student, but I do know that many English students have a short-sighted and completely utilitarian approach to this problem, and will not attend classes if there is not an examination in the subject concerned.

Although the present standing of paediatrics in our universities is a matter for congratulation, many of us have a feeling of shame that it has taken us over 100 years to follow the example of Sweden. On May 2, 1845, the paediatric clinic of the Royal Caroline Institute, Stockholm, was opened under the charge of Dr. Berg, the first professor of paediatrics; and every medical student was obliged to attend the course of instruction given by Dr. Berg, and an examination in the subject was compulsory.

This action by the Swedes was the result of a memorial prepared in 1842 by the professors of the Caroline Institute in which they stressed the difference between disease in infancy and that in adult life and the need for a clinic for children. As the greatest living Swedish paediatrician, Professor Wallgren, has said: "The words in which this memorial was couched heralded the dawning of a new day" in Sweden. In this country it was another nine years before, in 1851, the first children's hospital was opened in Liverpool, followed a year later by one in Manchester and one at Great Ormond Street, London.

*An abridged version of an address given at the opening of the Department of Child Health of the Welsh National School of Medicine at Llandough Hospital, Cardiff, on October 12, 1950. This was received for publication after Sir Leonard Parsons's much-regretted death on December 17, 1950.

Association with Obstetrics

Instruction in diseases of children was originally given by teachers of obstetrics, whose chief interest was in infants, but who, even so, were rightly more concerned with the mother than with the baby. The close association of paediatrics with obstetrics is of the greatest importance, as both during pregnancy and in the early months of infancy the mother and child are one biological unit. Paediatricians and obstetricians therefore must work in a close partnership, the paediatrician advising on the care of the foetus and child and the obstetrician caring for the mother. Only in this way can the present stillbirth and neonatal mortality rates be reduced to their proper proportions. Although here I am primarily concerned with the specialist, the same happy combination can and should exist between the general practitioner and the child-welfare medical officer, and the general practitioner can himself combine both roles.

It is interesting to me to realize that the first independent lectureship in children's disease was instituted in 1857 by my own medical school. This occurred before there was a children's hospital in the town. I do not know the reason for the appointment nor why, in 1868, it lapsed for a period of nearly 50 years. Manchester in 1881 was the next medical school to appoint a lecturer, and various others were appointed from time to time until 1932. The first paediatrician to be accorded professorial rank was Sir Frederic Still in 1906, but his position was only a titular one, as he was without any proper academic department. In those early days there was no question of co-operation with public health departments; nevertheless, I would like to put on record the fact that the resuscitation of the lectureship in 1915 in my own university—to which I was appointed—was due to the advocacy of a great medical officer of health, Sir John Robertson. At that time he was professor of public health, and he insisted that the title of the lectureship should be "Infant Hygiene and Diseases of Children." He was thus one of the pioneers, if not the actual pioneer, of the association between preventive and curative paediatrics.

Preventive Paediatrics

Preventive paediatrics was at first largely a voluntary effort, and its present position is chiefly due to the introduction of the school medical service, the creation of a Ministry of Health, and the foundation of the child welfare service. This series of events has been fraught with great benefits for the children of this country, but for many years it produced a great cleavage in paediatrics. Revelation is perhaps a better word than cleavage, because the development of these services revealed to many hospital paediatricians and general practitioners their neglect of a great part of paediatrics, that, in fact, they were concerned only with the child when ill and had little or nothing to offer in the way of advice on the upbringing of the healthy child or of the measures to be taken to maintain its health.

The development of these services, as we know only too well, resulted in the creation of two types of paediatrician: the one concerned with preventive paediatrics and who has little experience of curative work, and the other with considerable experience of curative and little experience of preventive paediatrics. This state

of affairs still exists, but happily it is being remedied largely by the creation of child health departments.

Twenty-five years ago I first visited Canadian and American paediatric centres. I said at the time, and I have never changed my opinion, that the paediatric department of Toronto was the best in the British Empire. I saw there, for the first time, that co-operation between preventive and curative paediatrics and between the public health and hospital authorities of which I had dreamed but which so far had indeed proved nothing but the "baseless fabric" of a vision. A municipal health visitor attended each out-patient department, heard the instruction given, and later visited the child's home to see if these instructions were being carried out. If a child did not attend the out-patient department when it should do so, a message to the public health department ensured a visit to the child's home to find out the reason. The milk kitchen of the hospital supplied special foods to children in their homes; the municipality provided a preventorium for child tuberculosis contacts which was staffed from the children's hospital, and this before we were familiar with the primary complex. The hospital also supplied consultant services to the infectious diseases hospital. In many other ways there was the most complete link between the municipal authorities and the hospital, which were closely united with other university departments both geographically and spiritually.

Child Health Institutes

On my return I tried, but without avail, to persuade my university to create a chair of paediatrics and to link up with the public health department. Three years later I was made a professor and also consulting physician to the municipal babies' hospital; but no closer connexions with the municipality occurred, although a further attempt was made in 1929. I consulted the late Sir George Newman, thinking at that time that the Chief Medical Officer to the Ministry of Health could direct municipalities to pursue a certain course, but I soon learned how mistaken I was. A third unsuccessful attempt was made shortly after war broke out; but in my wartime capacity as hospital officer I came into close contact with chairmen of public health committees and medical officers of health, and eventually in 1946, 21 years after my first effort, a scheme was agreed to whereby the university, the local authority, and the children's hospital united to form a child health institute. The scheme might perhaps be taken as a broad pattern for other child health departments, but details would obviously have to be modified to fit the particular university, board of governors, and regional board concerned. Up to the present all existing child health institutes are spiritual rather than material entities because there are no actual institute buildings. When an institute can be built in Birmingham it is hoped to erect it on land near the children's hospital, and it will become the headquarters of preventive paediatrics just as the hospital is the headquarters of curative paediatrics.

The child welfare, school medical, tuberculosis, and mental deficiency services have all been linked up with the university department, and certain members of the staffs of these services are university lecturers and certain others are clinical assistants at the hospital. The professor of paediatrics is consulting physician to the city child welfare service, and the registrars undertake duty as child welfare and school medical officers. In addition one of the hospital physicians conducts a consultative child welfare clinic in the city's largest child welfare centre.

University Child Health Department

It is obvious that although such a scheme confers great benefits upon both the university and the local authority it is limited in its scope because it is confined to the university town. Clearly, therefore, subsidiary child health institutes are required in other large towns in the region, and these should have a close connexion with the university. The professor and his chief assistants should pay regular visits to these outlying centres, and the people working in them should have access to the university department; there should also be an interchange of registrars. The board of governors of the teaching hospital and the Birmingham Regional Hospital Board have recently laid down as a condition of appointment of registrars that they must be prepared to work in other centres as well as the one to which they are primarily appointed. It is hoped by this means to effect an interchange of registrars between the teaching and the regional board hospitals. I notice that the Ministry has now recommended the general adoption of this procedure. There may sometimes be difficulties in this interchange, when, for instance, the outlying centres are a long way from the university town or if the registrar is married and has given hostages to fortune in the shape of children and ownership of a house; but in many instances a way can be found to overcome or minimize these difficulties.

Visits to outlying centres, the necessary administration of his department, and attendance at innumerable committees will consume a great part of the professor's time, but expenditure of time in this way seems unavoidable in the present structure of the Health Service. It is therefore essential that he must be assisted by an adequate staff; a staff which in the old days would have been beyond the bounds of our imagination. In addition to a number of consultant paediatricians it is necessary to have the help of skilled laboratory workers, pathologists, biochemists, etc., and, whilst in a general hospital these can be shared with other departments, there are advantages in having people specially trained to appreciate the paediatric standpoint. Such a university child health department will of course require a considerable income in excess of the normal cost incurred by the hospital in carrying out its primary duty—the care of the sick child. If staffed by whole-time officers this extra cost may reach £10,000 a year, a figure which has been accepted by the university grants committee. Where there is a close link-up with the local authority, such as I have suggested, it is reasonable to expect from it a substantial contribution to these running costs—as is done by the City of Birmingham.

Training in Paediatrics

Whilst the primary duty of such a department is the care of the sick child there should also be organized research into the cause, cure, and prevention of illness and the study of methods to ensure optimum health among the child population. In addition the university department of child health is responsible for the teaching of undergraduates and postgraduates. The standard of child health and the treatment of the sick child cannot be improved by any quicker or better method than by the adequate training of medical

students. This will ensure that the country possesses general practitioners who at any early stage in their career are capable of giving sound advice about healthy and sick children. In years gone by many practitioners have displayed little interest in the promotion of child health, and those who were interested had to a great extent to educate themselves.

According to the Goodenough Committee the teaching of paediatrics can best be developed "along the lines that child health and children's diseases constitute an important part of the training in general medicine and to a lesser extent in surgery, and that, in addition to a relatively intensive training in the subject, teaching on the health and diseases of children should run like a golden thread throughout the whole of the curriculum." Your new department will provide this intensive training and will, I feel sure, be able to count in particular on the departments of anatomy and physiology in carrying out the advice of the Goodenough Committee. It seems to me that it is wise to link together teaching concerning the function of an organ with its structure in order to show how, in the developing embryo, infant, and child, form waits upon function and function frequently dictates structure.

Paediatrics should also be a part of the transitional course which now intervenes between the preclinical subjects and full clinical studies. In this course the student should be informed of certain matters of which I have already spoken; in particular he should realize that to understand the natural history of many diseases he must study them in children, and he must also be instructed concerning the great importance of adequate nutrition and of environmental conditions in childhood. It seems to me that in no other department of medical study can curative, preventive, and social medicine be so intimately linked together and achieve such outstanding results as in the department of child health.

I have already stressed the close association which should exist between obstetrics and paediatrics: instruction on the care of the newborn child must form part of the intensive training of every medical student. Other aspects of this intensive training are clinical clerking, and attendance at child welfare, school medical, child guidance, and tuberculosis clinics, and at a mental deficiency institution. In the period of clinical clerking I hope it will be possible to carry out the suggestion of the General Medical Council and arrange for each student to reside in hospital for a period of four weeks. The condition of sick children, and particularly of sick infants, may change so rapidly that unless the student has the opportunity of observing these changes he will often be completely at sea when called upon to treat sick infants in his private practice.

The size of the department should bear some relation to the number of students, as each student should have at least four children under his care. The University Grants Committee thinks that a professorial unit should contain not fewer than 60 beds; beyond that figure the number of beds required depends entirely on the number of children needing in-patient treatment and the number of students. It is an ideal condition for the teaching of medical students and student nurses that the beds used for teaching should be all or nearly all in one institution.

In addition to clinical teaching some systematic teaching is necessary, and this is perhaps best achieved by a system of tutorial classes or seminars. This system not only allows more intimate association between teacher and student, but also spreads the burden of instruction between the professor, his assistants, and the registrars. Some teachers think that such instruction should take the form of set lectures. This may be true if the lecturer is really good, but I am sure the other system is better, although an occasional lecture on general topics by the professor or some other member of his staff, or by a visitor, is stimulating both to teachers and to students.

Recent Trends

So much for the changes which are taking place in the status and teaching of paediatrics; but, as in other branches of medicine, changes are continually occurring in the subject itself. In fact, paediatricians now talk a different language from the one which they spoke even ten years ago. A few specific examples will illustrate this trend.

When a resident at Great Ormond Street Hospital I was greatly interested in pyloric stenosis of infants, but when I started practice in Birmingham in 1910 my colleagues told me that the disease did not exist in that city. This statement was of course soon disproved, but prior to 1919, when the first Rammstedt operation was performed at my hospital, the death rate from the condition was 80%. The introduction of that operation reduced the mortality to 50% between 1919 and 1923. A very different state of affairs exists now. In a series of 102 cases treated in 1946 there was not a single death, and in 1948 out of 105 cases there was only one death; and the frequency of the condition seems to have increased to such an extent that over 100 cases a year are admitted to hospital. This remarkable change is due to some extent to improved surgical and anaesthetic technique, but much more has been accomplished by improved pre-operative and post-operative care and prevention of infections among hospital babies. Moreover, as a result of better medical education there is now a greater awareness of the disease among general practitioners; this leads them to recognize it before the baby has become a wasted infant.

Before the late war diphtheria was said to be the commonest cause of death among children of school age, but now, as the result of the immunization campaign started during the later years of the war, deaths from diphtheria are approaching negligible proportions and its incidence has greatly diminished. The control of diphtheria ranks with that of smallpox as the greatest triumph of preventive medicine in our country.

Antibiotics, which daily increase in number and potency, have revolutionized the treatment and symptomatology of infectious diseases, and in some instances their efficacy has even extended to virus disorders. They have brought the brightness of hope to the parents of children suffering from tuberculous meningitis when previously there was nothing but unmitigated gloom; and mastoiditis, once so frequent and so often fatal, is now infrequent and has been stripped of most of its terrors. Antibiotics are so marvellous in their action that frequently they are given when a child has a temperature, before any diagnosis has been made, and indeed they often prevent a diagnosis ever being made. In this way the practitioner may be tempted to become careless and not try to solve the problem set before him. Even so, on balance there is no doubt that the patient is better off than when more care was

taken to diagnose the disease but there were less efficacious means of combating it.

In addition to antenatal paediatrics and the care of the newborn and premature infants perhaps the most recent general trends in paediatrics in the United Kingdom are the adoption of the Gesell technique in the study of the development of the baby, and an assessment of the pattern of growth by such means as the Wetzel grid and the Tuxford index. These are attempts to decide the normal; but what is the normal?

A good knowledge of the abnormal, especially in its minor degree, is important for a knowledge of the normal, and therefore a wide experience of curative paediatrics is essential even to those engaged in preventive paediatrics. Most of the data which we now accept as normal—particularly, for example, in regard to heights and weights at various ages—are averages and not normal. Normality usually covers a wide range, but if there is an optimum level which can be obtained it should surely be regarded as normal. An excellent example of the point I am trying to make is found in the haemoglobin values of babies. Helen Mackay and others have shown that the values which we had previously regarded as normal could be raised, particularly in artificially fed infants, by adequate supplies of iron, and could even be improved by giving iron to pregnant women. Children with this higher level of haemoglobin were found to be better nourished and to stand infections better than those not given iron. Therefore it seems to me that this optimum figure ought to be regarded as normal.

Conclusion

Whilst composing this address I was on holiday in North Wales, and during a walk on a fine day I was entranced by the effect of sunlight and shade on the mountains in contrast with the complete shadow of the foreground. The country in the foreground was lovely, but in the sunshine the loveliness was greatly enhanced, the colouring far more attractive, and the whole effect wonderfully different. It seemed that here was an analogy which explained my ideas: the foreground was the "average," and the sunlit landscape the "optimum." Only the "optimum" is good enough for our children, and this should be the goal for which we strive. Actually, I think we are in process of achieving it, because children in all classes of society are obviously more healthy and better nourished than they were before the war. For this change the health services and paediatricians deserve a greater share of praise than politicians, and the latter a much smaller share than they are wont to arrogate to themselves.

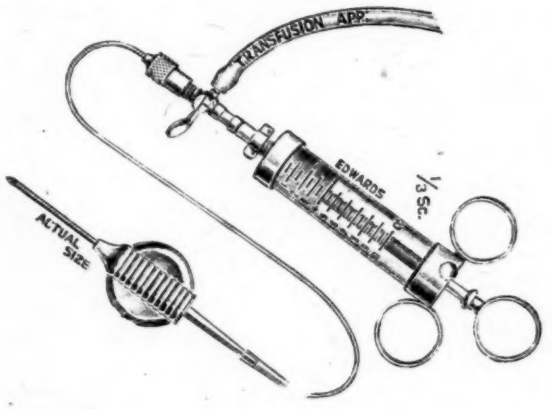
H.M. Hospital Ship *Maine* was the only hospital ship on the Far East station at the outbreak of war in Korea, and until October, when she returned to Hong Kong, she was engaged in evacuating wounded and on general hospital ship duties. The 7,514-ton *Maine* was formerly the Italian *Leonardo da Vinci*, and was converted into a hospital ship in 1943. In March this year Denmark sent the 8,500-ton *Jutlandia* to Korea. She carries 16 doctors, 40 nurses, and 25 medical aid men, all of whom are volunteers. There are four specially designed operating-rooms, and 300 surgical cases can be handled; many of the complicated cases from Korea will be sent to the ship for treatment. The beds are fastened on rockers so that they remain level when the ship rolls, and extra wide beds have been installed for fracture cases.

Preparations and Appliances

APPARATUS FOR SCALP VEIN TRANSFUSION

Dr. J. J. KEMPTON, paediatrician, Royal Berkshire Hospital, Reading, writes: The new design of needle described below has seemed to have some advantages over previous apparatus for transfusion by scalp vein.

The scalp vein needle consists of a small flanged mount, a needle shaft 11/16 in. (1.75 cm.) in length, with a 45-degree bevel point, and a short tapered shaft on the proximal end of the mount, to which polythene tubing is connected. The under side of the flanged needle mount is shaped to lie flush on the infant's scalp while the needle is within the vein, and may be secured in position with adhesive strapping. A set of three needles of 24, 25, and 26 B.S.W. gauge provides a choice equivalent to hypodermic-needle sizes Nos. 15, 16, and 17.



The side branch stopcock is equipped with a polythene tubing adaptor which grips the wall of the tubing by compression of a rubber gland. A screw mount on the proximal end of the stopcock ensures a secure attachment to the syringe, which is of the three-finger-ring type with a screwed nozzle for mounting the stopcock. Both the syringe and the polythene tubing adaptor are similar to those described in connexion with exchange transfusion apparatus by Dr. John Henderson (*Lancet*, 1950, 2, 291).

A length of polythene tubing is mounted on the tapered shaft of the needle and connected to the stopcock by means of the screw-on polythene tubing adaptor. The tubing from the standard blood-transfusion-giving set is connected to the side branch of the stopcock, and the stopcock is screwed on to the nozzle of the syringe, which is of either 10-ml. or 20-ml. capacity. Blood can be seen to enter the polythene tubing when the needle has entered the vein; the syringe is then filled with blood from the giving bottle and injected into the scalp vein of the infant. At the outset, needle and tubing contain saline.

By the above means flexibility is achieved between the infant and the syringe, and the necessity of holding anything more than the scalp vein needle against the infant's scalp (such as a Kaufman syringe) is overcome. At the same time polythene tubing provides an excellent window through which blood can be seen immediately the needle is passed into the vein, and air bubbles are similarly readily detected.

Saline infusions may be given by the gravity drip method, using the components described, but in this case the syringe and stopcock can be discarded in favour of a simple polythene tubing adaptor equipped with a female Record tubing mount.

The apparatus has been made for me by Edwards Surgical Supplies Ltd., 83, Mortimer Street, London, W.1.

Correspondence

Anterior Pituitary and Toxaemia of Pregnancy

SIR,—I have read the articles on the subject of cortisone and the subsequent correspondence with great interest, particularly the suggestion (May 5, p. 1016) that toxaemia of pregnancy may be associated with hyperactivity of adrenals due to stimulation by the anterior pituitary. One of the difficulties in the study of toxaemia of pregnancy is the differentiation of the various types of hypertension occurring in pregnant women, and much of the controversy would be resolved if care were taken in the choice of cases for study.

In this department we have been able to show that there is a certain group of cases in which there is apparent hyperactivity of the anterior pituitary. This was first suggested to us by the results of a study of foetal ovaries in stillbirths arising in cases of toxaemia (Govan and Mukherjee, 1950). Subsequent studies have shown that the gonadotrophins in this type of case are capable of stimulating the testes of immature and hypophysectomized adult male rats, which is a fair indication that the gonadotrophins are of pituitary origin. The hypertension in this group appears to be of humoral origin according to the results obtained with tetraethylammonium bromide. In addition, they show a negative nitrogen balance (Mukherjee and Govan, 1951) and they are insensitive to the action of insulin (Govan *et al.*, 1951). These results provide additional evidence for the hypothesis that there is a hyperactivity of the anterior pituitary in this group of cases. It is difficult, however, to determine which of the many hormones is actually responsible for the changes, since any alteration in the secretion of one hormone inevitably leads to secondary changes in the activity of other hormones. However, our results in the examination of tissue fluid from these cases (Mukherjee and Govan, 1950) indicate that there may be an upset in the carbohydrate metabolism of the tissues. We have found that the oedema is mainly associated with an increase in the organic acids and phosphates in the tissue fluids. There is a retention of sodium, and although this may be active in nature we are rather inclined to believe that it is secondary to the retention of acid substances. Contrary to the suggestion of your correspondent (Dr. R. Schuurmans, May 5, p. 1016), we found that there was a very low protein content in the oedema fluid, a fact which disproves any general increased permeability of the capillaries. Albuminuria in these cases may be related to the local circulatory changes in the kidney or even to the more intimate changes in metabolism.—I am, etc.,

Glasgow. A. D. TELFORD GOVAN.

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Confidential Papers and the State

SIR,—Dr. S. Barton Hall may have performed a great service to both patients and doctors by raising the issue of professional secrecy (May 5, p. 1020). Before others consider possible methods of meeting the moral evil noted by Dr. Hall, it might be useful to note briefly certain aetiological factors in the problem.

The National Health Service Act, by making practically all doctors full-time servants of the State, put an end to the confidential relationship between doctor and patient. There is nothing new or startling in this—it is a point which was underlined time after time by many members of the profession before the introduction of the Act. When there is a clash of interests between the patient and the State you cannot serve both. The case-sheets of the hospital consultant and the record cards of the general practitioner are the property of the State, not of the doctor, and therefore no longer confidential. The recent circular of the Ministry of Health is the logical sequel to these two points. The circular is for the guidance of *lay* hospital administrators in the use to which they can put patients' case records. The problem is therefore beyond the control of the individual doctor so far as *existing* case records are concerned. In these cases the principle of professional secrecy has already been surrendered.

The Beveridge Report and the National Health Service Act were based on the German philosophy (implemented by social legislation from Bismarck's time to Hitler's) that the State is all and the individual nothing. The doctor is the tool of the State, and no longer the servant of the patient. For the moment, apart from stating that the only radical solution of this ethical problem is the abolition of the Health Act in its present form, I will leave the suggestion of first-aid solutions to others. Finally, I wish one sentence of Dr. Hall's letter could be given front-page publicity in all our national newspapers:

"It is small wonder that it is becoming increasingly common for new patients to ask whether the interview is confidential, or to request that written notes of their story shall not be made."—I am, etc.,

Woodford Green, Essex. LEO P. GRAY.

SIR,—Dr. S. Barton Hall (May 5, p. 1020) is trying to place the question of medical confidence on an idealistic plane. How confidential is a medical history which is related in minute detail in an open court of law with reporters present? No one can object to that if the information is required in order to arrive at a just legal decision. How confidential is the average patient's medical history when it is discussed by the patient with his or her friends over a cup of tea or a pint of beer? He or she likes doing this, and, moreover, it is the most popular pastime in this country.

I have been a member of a Ministry of National Insurance Medical Board since the inception of the National Insurance Act, and can say that the details of a claimant's medical history, which can be obtained only from his hospital notes, are absolutely necessary in order to arrive at an accurate estimate of his degree of disability, and are treated completely confidentially as between one member of the medical profession and another. Furthermore, I have yet to hear of any claimant being aggrieved because his hospital medical history has been made available to the members of such a board. In fact, the more information available, the more the claimant likes it—he is not worried about any breach of professional confidence. Taking Dr. Barton Hall's hypothesis to its logical conclusion, when he sees a patient who requires any further investigation, say a pathological investigation, he must not see the pathological report on his patient because it would be divulging information and would not preserve medical confidence, as he puts it, which of course is completely absurd.—I am, etc.,

King's Lynn. P. G. E. JOLLEY.

Prescribing Potassium or Sodium Bromide

SIR,—The recent announcement (April 28, p. 963) that sodium bromide might be dispensed by chemists in place of the potassium salt when supplies of the latter are not available to meet N.H.S. prescriptions should receive the widest publicity among doctors.

Those with congestive heart failure, hypertension, oedema of pregnancy, or obesity are frequently ordered a salt-restricted diet. If, at the same time, the doctor should prescribe one of the several mixtures containing potassium bromide and the chemist supplies the sodium salt, the intake of sodium ion is likely to be sufficient to defeat the purpose of the diet. In such circumstances, doctors should endorse their prescriptions "Not sodium bromide."—I am, etc.,

Woldingham. L. M. SPALTON.

Conception and Oligozoospermia

SIR,—We would like to answer Dr. P. M. F. Bishop's letter (April 21, p. 882). Our object (April 7, p. 741) was to illustrate the fact, not generally recognized, that pregnancy can take place even in couples where the husband suffers from extreme oligozoospermia, and to persuade the practitioner to refer such cases for further investigation in order that every chance may be given them. Dr. Bishop implies that such cases can be treated only by specific and unavailable hormone preparations. He must be unaware of the extensive biological and medical literature which shows that a large number of unspecific factors can impair testicular function (cf., e.g., Lagerloef, N. (1934), *Acta path. microbiol. scand. Supp.* 19; Imig, C. J., Thomson, J. D., and Hines, H. M. (1948), *Proc. Soc. exp. Biol., N.Y.*, **69**, 382; Yamasaki, Y. (1923), *Virchows Arch.*, **245**, 513; Bretschneider, L. H. (1948), *Nutr. Abstr. Rev.*, **17**, 966, abstract No. 4832; Brown, S. O., Wilkening, M. C., and Schweigert, B. S. (1948), *Proc. Soc. exp. Biol., N.Y.*, **68**, 672; Mills, R. G. (1919), *J. exp. Med.*, **30**, 505; Morgenstern, Z. (1923), *Virchows Arch.*, **245**, 229; Stieve, H. (1925), *Z. mikr.-anat. Forsch.*, **2**, 598, and **12**, 233 (1927–8); MacLeod, J. (1946), *Conference on Diagnosis in Sterility*, ed. Engle, E. T., Oxford), and that it is the first duty of the physician to eliminate nutritional and other adverse conditions affecting general health. Again, neither impairment nor improvement of fecundity is always reflected in the sperm count; and this must be borne in mind when estimating the effect of treatment (cf., e.g., Moench, G. L. (1931), *Z. Geburtsh. Gynäk.*, **99**, Supplement.

While it is not possible here or in a memorandum to give full details, it is surely obvious that treatment of semen showing signs of infection requires antibiotics (Case 1), that liver is a recognized source of accessory nutritional factors required for optimum fertility, and that it is not necessary to weigh exactly the protein intake of any patient where common sense and careful inquiry have revealed a protein deficiency according to ordinarily accepted standards. There are many cases where faulty or careless food habits do in fact produce a continuous slight deficiency in first-class protein. Even within the limits of present food supplies and allowing for rationing, there are many people who do not plan the use of available food to their own advantage, and we endeavour to help both husband and wife in this respect. Other treatment such as the administration of iron and arsenic followed general medical principles and does not require specific explanation.

We ourselves pointed out the importance of compensating fecundity in the wife, and even if nothing else can be done it is for this reason alone worth referring such couples for full investigation. In Case 1 no conception could have occurred until after the wife had received attention. It is a remarkable fact that it occurred even then, for a semen test taken before the second conception occurred showed persistence of extreme oligozoospermia (after one week's abstinence: volume 4.3 ml., 0.05 million sperms per ml., 75% abnormal forms, 20% fully active after one and a half hours at 37° C., 10% fully active after three and a half hours at 37° C.). This observation answers Dr. Bishop's remarks concerning the spermatogenic status of the husband at the critical time.

Concerning other questions raised by Dr. Bishop, such as timing of post-coital tests and correction of coital technique, it is surely not necessary to explain that this clinic has not abandoned the precautions commonly observed by all experienced workers in this field. To tell an infertile couple that there is "no effective treatment yet available for defective spermatogenesis" seems to us too narrow and categorical a statement and likely to cause unnecessary loss of hope, whereas our plea for a guarded prognosis coupled with any and every effort to make conception more likely is at least the patient's due.—We are, etc.,

MARGARET MOORE WHITE.
MARY BARTON.

London, W.1.

Electro-convulsive Therapy in a Patient with a Major Fracture

SIR,—This note is a report of the administration of E.C.T. to a patient with a fracture of the femur, when the broken bone was immobilized in a Thomas's splint under traction and suspended from a frame.

A woman of 36 was admitted on November 20, after having fallen under an electric train. She was conscious but severely shocked, and had a retrograde amnesia of about six hours. Examination showed that she had a simple fracture of the mid-shaft of the right femur, a fracture of the left clavicle, a fracture of the lateral epicondyle of the right humerus, and severe bruising of the right orbital region with multiple abrasions. She was treated for shock and transferred to the fracture ward; the fractures were immobilized, the femur in balanced traction, the clavicle with a figure-of-eight bandage, and the right elbow in plaster-of-Paris.

Her physical state seemed to be satisfactory, but she had signs of depression, and inquiry from witnesses indicated that her injuries were the result of an attempt at suicide. Her mental state did not improve, and Dr. John B. Randell was asked to see her. He considered that she was gravely depressed, retarded, and preoccupied with ideas of self-reproach, and recommended a course of E.C.T. Five treatments were given between January 17 and 30. The fractures were showing no callus at this time, but early clinical union was present.

Atropine sulphate 1/75 to 1/50 gr. (0.87–1.3 mg.) was given subcutaneously thirty minutes before inducing anaesthesia. 180 to 200 mg. "flaxedil" and 0.5 g. thiopentone were then given intravenously. The lungs were intermittently inflated with oxygen by means of a Boyle's machine before the shock was given, and afterwards until adequate spontaneous respiration was resumed. A Phillip's pharyngeal airway was inserted, which, besides keeping the airway perfectly clear, also acted as a gag to prevent tongue-biting. The electro-convulsive shock was given three to five minutes after the flaxedil injection. 2.5 mg. neostigmine was given intravenously five to ten minutes after the shock.

With 180 mg. flaxedil, double the dose which produced respiratory arrest in this patient, movement of arms and legs was not quite prevented when the shock was given, though the fractured femur was not affected. On all subsequent occasions the dosage of flaxedil used was 200 mg., which produced complete immobility, except that the muscles of the head and neck still contracted slightly. Atropine (1/75 gr.) was given before the first two treatments. On the second occasion only a Magill endotracheal tube was passed, but shortly afterwards an excessive mucous secretion was found in the pharynx. On subsequent occasions the dose of atropine was increased to 1/50 gr. and a Phillip's airway only was used.

A short attack of hiccups preceded the return of respiration on the fourth occasion. Nothing else abnormal occurred and there was little change in the pulse rate or blood pressure following the injection of flaxedil and thiopentone. Adequate respiration was resumed within 20 minutes of giving flaxedil, but the return to full consciousness was preceded by a confusional state lasting one to two hours.

During shock therapy no alteration in the position of the fracture occurred, and the bone progressed to sound union, clinically and radiologically, by 15 weeks. After E.C.T. the depression and retardation had entirely cleared, and the patient said she felt quite different. Her relatives told us that they thought she had returned to her normal self.

—We are, etc.,

London, W.C.2.

CYRIL F. PRIDEAUX.
JOHN E. BUCK.
DESMOND O'NEILL.

Relaxants in Electro-convulsive Therapy

SIR,—The two papers on the modification of E.C.T. by gallamine triethiodide ("flaxedil") by Mr. O. S. Thompson and Dr. A. Norton (p. 857) and Drs. R. H. F. Smith and D. L. C. Thomas (p. 860) in your issue of April 21 prompt me to quote my experience. I have used D-tubocurarine and C10 for this purpose for several years (Coffin, 1949, *British Medical Journal*, **1**, 1050, and Coffin, 1951, *Anaesthesia*, **1**, 58), and, having experienced in surgery the benefits of the reduced respiratory depression from "flaxedil," I have

more recently used the latter as a relaxant in E.C.T., and because of this property find it an improvement over the former two drugs.

The relative doses seem to be: D-tubocurarine 15 mg., C10 3 mg., and flaxedil 75 mg. I find the dosage of flaxedil, when used to modify E.C.T., is best estimated at 9–10 mg. per stone (6.3 kg.) body-weight for the average patient, slightly less than this being given for the first treatment until the response has been discovered, and still less for the elderly. I always ventilate with oxygen for two minutes, by which time relaxation should be satisfactory, and aim not at complete immobility but at the slightest or no movement of the trunk with slight flexion of the forearms.

I am of the opinion that it is better not to mix the relaxant with the thiopentone. Used separately through the same needle one can more accurately judge the minimal amount of thiopentone needed, and the change-over of syringes should not, with experience, cause any displacement of the needle. The atropine should be mixed with the relaxant, not with the thiopentone, as the latter mixture is, in my experience, a likely cause of venous thrombosis (Hunter, 1948, *Anaesthesia*, **3**, 116), especially when many venepunctures have to be made as in a course of E.C.T.

The giving of a relaxant without thiopentone seems to me unjustifiable. With the present accumulation of experience of using relaxants in E.C.T. it is quite unnecessary, and I am glad to see that it has been abandoned.—I am, etc.,

London, W.1. STEPHEN COFFIN.

Hiccup and Hexamethonium

SIR,—Hexamethonium abolishes the "lobeline cough" (*Glasgow Medical Journal*, 1951, **32**, 72), apparently blocking a carotid sinus reflex. Therefore it seemed probable it might affect a reflex such as hiccup, and it was administered by injection to a patient with a persistent attack. The hiccup ceased almost immediately thereafter. No further opportunity has arisen to confirm this observation, and we note with interest Dr. McGill's account of a similar result (April 28, p. 948). In a child with whooping-cough a single attempt was made to control the paroxysms with hexamethonium, but they were not alleviated in this instance.—We are, etc.,

B. R. HILLIS.
Glasgow. J. C. C. KELLY.

Foetal Asphyxia

SIR,—The fact that the lungs of the newborn are collapsed and airless is no doubt responsible for the assumption that the initial respiratory effort must needs be inspiratory. Strange as it may seem, the infant's first attempt at respiration is always expiratory. The phenomenon is best observed as a marked increase in tonus of the abdominal muscles and culminates in a faint convulsive-like spasm or shudder. The physiological explanation for this behaviour on the part of the newborn is bound up with the problem of mobilization of the afferent circulation. A local effect may be to clear the air passages of amniotic fluid. A nasal discharge appears before the first inspiration, and perhaps some fluid is swallowed, for investigators have found evidences of alimentary activity before any signs of lung inflation.

The circulation in the newborn must necessarily undergo a rapid and complex adjustment. None of the factors said to be responsible for the venous return in the adult can play any part in the initial mobilization of the infant. These are the respiratory suction aided by the pressure action of the abdominal muscles on the viscera and the movements of muscles pressing on the veins. Were this the true explanation voluntary hyperpnoea should (but does not) improve the pulse pressure. Where a true circulatory asthenia exists forced breathing may induce untoward effects such as tetany, or aggravate the signs and symptoms of the effort syndrome (neurocirculatory asthenia). In fact, hyperventilation resulting in a gaseous alkalosis is a feature of some neurotic and hysterical states. Again, apnoea in expiration, whether voluntary or such as is produced by adrenaline, normal physical effort, the therapeutic convulsion or the epileptic fit, should by reducing the intrathoracic pressure and the respiratory suction action also reduce the venous return to the heart and thereby reduce the output of the left ventricle. But this is far from being the case. Apnoea leads to an increase of CO_2 tension, and a measure of success has in recent years been claimed for the therapeutic use of inhalations of this gas in some psychopathic states.

Undoubtedly the problem of the venous return is in need of further investigation. Its importance is evidently not realized if one is to judge by the scanty attention it receives when compared with that devoted to cardiology and the arterial side of the circulation. Since the left ventricle is dependent for its output on what it receives from the right ventricle by the way of the pulmonary circulation, and the right, in turn, can supply the lungs only with what it receives from the great veins, it is obvious that the mechanism responsible for the venous return is the dominant factor in circulatory supply.

The venous return depends, I believe, on a single, kinesiologically accessible factor, which, for want of a better term, I will call the "faculty of vacuolation" of the organism. The intra-abdominal pressure is normally negative, a negative pressure that is undoubtedly increased in proportion to the degree of effort. During vigorous muscular effort, when the demands on the circulation are at their highest, the abdominal wall becomes markedly retracted or scaphoid in appearance. In addition the muscles of the athlete in action stand out: in other words the skin is sucked in along the muscle margins. This suggests an inter-muscular negative pressure. This faculty of vacuolation, to my mind the most vital of all the body mechanisms, reaches its developmental acme during athletic prime, its power gradually waning with advancing years. The skin tends to become loose, wrinkled, and apparently somewhat redundant in old age.

A study of the movement responses of athletic subjects to an effort stimulus and of the underlying physiological adjustments in the adaptation for physical effort helps to explain how the increase in intra-abdominal negative pressure is brought about. The immediate objective response, probably the same in all vertebrates, is always an extensor movement. Now expiratory movement always synchronizes with the extensor movement. The attachment of the spinal muscles to the ribs confirms this, and, incidentally, throws new light on the still problematical role of the internal intercostals in respiration. Where effort superimposes effort the response is the same. One has only to witness a horse take a fence to note the increased back-stiffening and hear the accentuated expiratory effort. The volume of the abdominal viscera is reduced by the blood-shunt to the muscles. Thus, three factors come into play in increasing the intra-abdominal negative pressure. The extensor response elevates the thorax and braces the pelvis backwards; this stretches the abdominal muscles and eliminates sag. The associated expiration raises the diaphragm and with it the abdominal viscera. The reduced volume of the latter tends to draw the abdominal wall inwards.

Barcroft (*British Medical Journal*, 1939, **2**, 986) investigated the intrauterine development of respiration in the sheep. He describes the results of a stimulus to the foetus as a somatic response, extensor in type, followed by a respiratory response, the three factors concerned (the stimulus, the immediate somatic response, and the following respiratory response) being related quantitatively. I have not seen the film referred to by Dr. W. N. Leak in his letter (February 3, p. 246), but I am convinced that what Barcroft described as the respiratory response was actually inspiratory in type. He evidently overlooked the fact that the preceding extensor response was also the expiratory phase of respiration.

My experience of asphyxia in the newborn is very limited, but I believe it to be due to weakness or fatigue (due to protracted labour) of the "faculty of vacuolation." Respiration would be of little use without a blood supply to the lungs.—I am, etc.,

Callan, Co. Kilkenny. WILLIAM HERON.

Orf in the Country

SIR,—The series of cases of orf occurring among Smithfield porters, described by Dr. I. S. Hodgson-Jones (April 14, p. 795) shows some clinical variations from those occurring in a rural area among agricultural workers. This is probably accounted for by their outdoor employment. Nine cases have been recorded by me since the war years, when time did not allow for adequate observation of earlier cases.

In no case has the dead, white, soggy skin been seen except where marked secondary infection has supervened. Lymphangiitis has not been detected until the vesicle has been broken, so that one has come to regard it as associated with secondary infection. Generally, a single lesion is seen, but cases have occurred where the primary lesion has remained small and a circinate group of secondary lesions have broken down, simulating the classical illustration in the older text-

books of malignant pustule. These multiple lesions have been seen only where the patient has applied dressings prior to seeking advice.

The site of the lesion in the adult cases has generally been on the hands and forearm; predominantly on the hands and more usually on the dorsal aspect. The case described recently (G. M. Lloyd, A. Macdonald, and R. E. Glover, *Lancet*, 1951, **1**, 720) illustrated a case where the brow of an adult was infected. Other facial lesions have always occurred in children, as reported by Dr. A. K. Rankin (*British Medical Journal*, 1950, **2**, 1279). Once again two small girls with pet lambs have been seen with lesions on the lip and the temple respectively. The first post-war case was that of a farmer's schoolboy son who developed orf on his upper eyelid while bottle-feeding a lamb which had lost the ewe.

The condition resolves itself in five to eight weeks, as reported. Treatment with the earlier antibiotics has been unsatisfactory. Chloramphenicol and aureomycin have not been available in rural practice up to date. The sulphonamides have helped only to limit secondary infection. Very hot bathing, where assiduously applied after removal of scabs, has helped to shorten the course to about three weeks. Flavine in glycerin has been less useful. Zinc chloride (10%), as used by veterinary colleagues, has not had sufficient trial. If the eschar is repeatedly removed it appears beneficial, but it produces much soreness and the patient does not readily co-operate, though it would appear the most economical form of treatment.

Orf does not appear to penetrate the skin of the adult outdoor worker readily. There is usually a history of the worker having been recently employed in hedging, or retrieving the lamb from brambles and briars. No case of recurrent infection has been seen where the farm worker has in subsequent years handled infected sheep or lambs, so that immunity appears to be acquired.

The seasonal factor is apparently that of lamb-rearing, when stock are most frequently handled. Cases seen here have occurred between April and June and exceptionally as late as August.—I am, etc.,

Ross-on-Wye. G. M. LLOYD.

Pink Disease

SIR,—I was very surprised to read in the *British Medical Journal* (April 28, p. 933) that treatment of pink disease with the use of salt and desoxycorticosterone had not met with success. I have had two cases of pink disease in my practice which were very successfully treated by giving 120 gr. (7.2 g.) salt daily and 3 mg. desoxycorticosterone acetate on alternate days, with a total of five injections. The response was almost immediate. The irritability and insomnia started to disappear and the appetite improved. About ten days later the redness of the hands and feet started to fade away. It is now over three weeks since treatment was started and the tachycardia has practically disappeared, along with most of the other symptoms and signs.—I am, etc.,

Manchester. H. FORMAN.

Kimmelstiel–Wilson Syndrome

SIR,—Dr. Ian Gilliland's paper (April 28, p. 916) might have made clearer reading if he had defined his renal pathological groups more precisely. The use of the term arteriosclerosis without further definition or description is always confusing. We are told that in Group 1 (the Kimmelstiel–Wilson group) there is a pronounced degree of arteriosclerosis, and that this may be seen to affect both afferent and efferent arterioles. From these statements it must be implied that Dr. Gilliland includes arteriolosclerosis within the term arteriosclerosis, so that presumably Group 3, the arteriosclerotic group, includes kidneys showing arteriolosclerotic lesions and therefore overlaps Group 2.

It is generally considered that chronic hypertension is almost always associated with a significant degree of renal arteriolosclerosis. One is therefore surprised to find in Table IV that hypertension was present in only one of the three cases in the arteriolosclerotic group, in all three of the arteriosclerotic group, and in four of the "other diabetics" group, which by definition is free from renal vascular disease. This apparent lack of correlation between hypertension and renal pathology in the cases without Kimmelstiel–Wilson lesions also suggests that his various groups are far from clear cut.—I am, etc.,

London, S.E.5. G. F. M. HALL.

Industrial Health Investigations

SIR,—Your correspondents, Drs. R. S. F. Schilling (April 7, p. 759) and Alex. Mair (April 28, p. 950), comment upon industrial health investigation. They both refer to the work which requires physical examinations. I would point out that observations of less direct clinical interest, but not of minor importance, can be made from an examination of working methods. I think that the attitude to health in the lay mind has still a long way to go. You were kind enough to illustrate an arc-welder's shield which I designed (*British Medical Journal*, 1945, **1**, 154). A foreman fitter-

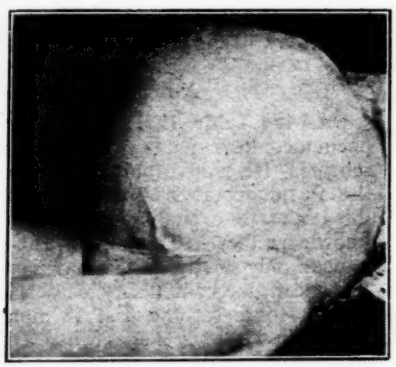
welder had been engaged in the old-fashioned practice of doing overtime in order to complete some construction. His enthusiasm had exceeded his discretion, and a very high voltage had been used. The next day his assistant presented himself with a typical "arc-eye." I felt that the routine methods would merit observation, and found that, although the welders themselves were adequately protected, their assistants, like the retainers of the knights of old, did not wear armour, and were therefore exposed to radiation.

The difficulties encountered arose not from the complexity of the problem but from the workers (I use the word in its modern elastic sense), who disliked being watched. One skilled artisan encompassed the attitude of the industrial worker with the words, "I'd rather have the danger money."—I am, etc.,

Rossendale, Lancs. J. NOEL JACKSON.

Enormous Ovarian Cyst

SIR,—To surgeons in the Tropics colossal fibroids and ovarian cysts are everyday fare, as Professor R. J. Last has indicated (March 24, p. 622). It was therefore with some surprise and pleasure that I met again two old friends whose photographs I append. They were both admitted to hospital



within a few days of each other during the flying-bomb era, because their relatives refused to stay and tend them any longer. They were both Christian Scientists, and neither of them had left their single rooms for over a year. Both had multilocular pseudo-mucinous cysts, the one containing 76 pints (42 litres), the other 60 pints (33 litres) of brown glairy fluid. After slow decompression-tapping, removal of the cysts was easy except for some parietal adhesions. Blood transfusion was unnecessary, but both were given two pints (1,100 ml.) of plasma during operation. They have both been seen quite recently, well and happy.—I am, etc.,

London, W.1. V. B. GREEN-ARMYTAGE.

Combined Penicillin and Streptomycin

SIR,—The recent paper by Dr. J. E. Cates, Professor R. V. Christie, and Professor L. P. Garrod (March 31, p. 653) on the treatment of penicillin-resistant bacterial endocarditis with penicillin and streptomycin prompts me to record the following case.

An accountant aged 37, with rheumatic mitral and aortic valvular lesions, was taken ill with "'flu" about the middle of November, 1950. As his pyrexia did not subside he was admitted to hospital on December 1 as a suspected case of bacterial endocarditis, a diagnosis which was confirmed on December 4 by culturing *Streptococcus viridans* from the blood stream. The organism was reported as penicillin-sensitive, so parenteral penicillin therapy on the usual lines was instituted on the same day. Owing to an error of prescribing he was given at the start even larger doses than is customary, and between December 4 and January 15 received in all 165.6 million units penicillin. The clinical response seemed excellent, but within 48 hours of stopping the penicillin his temperature rose, and on January 17 blood culture again produced a heavy growth of *Str. viridans*. However, the organism was reported as streptomycin-sensitive, so on January 22 daily intramuscular treatment was begun with 2 g. streptomycin and 12,000,000 units penicillin. This dosage was continued until April 17, so that in 12 weeks 168 g. streptomycin and 1,008 million units penicillin were given.

The final result seems to have been satisfactory. At the time of writing the patient has been apyrexial and symptomless for 20 days, and is beginning to get up and about. The likelihood of relapse seems small after such a period. There have been no symptoms or signs of labyrinthine damage by the streptomycin, and at no time has there been any cardiac decompensation.

It would be unwise to draw any rigid conclusions from a single patient, but as such cases of penicillin-resistant endocardial infections are rare one may perhaps be permitted to comment briefly. Cates, Christie, and Garrod treated their patients with larger doses of streptomycin and penicillin, but for a shorter period. In both their cases which survived there was labyrinthine damage due to the streptomycin. It is possible that this complication may be avoidable by less heavy but more prolonged dosage, as in the present case. In considering the length of time treatment should be given it is interesting to note that my patient, a highly intelligent man, volunteered the information that although he never had, while under treatment, any definite symptoms he could describe clearly, he did not feel entirely well until he had been on penicillin–streptomycin for about eight weeks. It seems therefore possible that the infection was not eliminated until that point, in which case it would appear desirable, if the described dosage is used, to continue treatment for at least this time—I am, etc.,

Adwy, nr. Wrexham. J. R. FORBES.

Spontaneous Rupture of Tendon

SIR,—A case of spontaneous rupture of the extensor longus pollicis tendon which I treated in 1937 may be of interest in confirming the view that this condition is due to a vascular necrosis rather than to friction, and in this way to support the view expressed by Mr. David Trevor (April 28, p. 952). A further point of interest was that in my case there was no fracture.

A man, aged 24, gave a history that he had cut his forearm postero-laterally about 3½ in. (9 cm.) above the wrist-joint six weeks before I saw him. There was a healed scar less than 1 in. (2.5 cm.) long, but the history was that the cut had gone very deep. Shortly before I saw him he had suddenly lost the power of extension of the thumb. I explored the extensor tendon and found that it had the typical soft yellow appearance near the site of the rupture which is seen occasionally following a Colles's fracture. There could be little doubt that the original penetrating injury had interfered with the blood supply going down from the muscle to the tendon.

Mr. Trevor advises end-to-end suture, but, owing to the extent of softening in the tendon in this and in some other cases that I have treated, it has been necessary to perform a tendon anastomosis. I personally prefer to suture the extensor carpi radialis longus to the distal end of the extensor longus pollicis tendon, as this ultimately gives an almost perfect result. In this particular repair it is interesting to note that re-education may be rather slow, as the extensor carpi radialis longus normally contracts synergically with the flexors of the hand and wrist.—I am, etc.,

Farnham, Surrey. STANLEY C. RAW.

Atropine and Whooping-cough

SIR,—Following on Dr. Stanley Banks's Refresher Course article on whooping-cough (March 31, p. 689) it is interesting to note that there has been a marked increase in this area in the use of atropine methyl nitrate in alcoholic solution: mostly in the form of the proprietary preparation "eumydrin." Apart from the question of its usefulness in

the treatment of whooping-cough, there is one point which should be borne in mind when prescribing it. We have already had one case of atropine poisoning in an 18-month-old baby who swallowed the contents of a 10-ml. bottle. If eumydrin is prescribed it would be safer, for *home* use, in the aqueous solution.—I am, etc.,

Colchester. ELEANOR M. SINGER.

POINTS FROM LETTERS

Cortisone and Toxaemia of Pregnancy

Mr. R. H. PARAMORE (Rugby) writes: Since the brain of the healthy primigravida in the mid-period of pregnancy so often shows a heightened activity, while if toxaemia appears as the pregnancy advances it becomes impaired or even deranged, might we not argue that some change in the brain is the cause of the disease? Should we be unwarranted then in suggesting the injection of cerebral extract; and in demanding of chemists the synthesis of such a substance? Would not such a substance be of value in the non-pregnant—e.g., for students preparing for an examination—or even in the treatment of mental deficiency? To say that the latter depends on aberrant structure is beside the point: no one dealing with women the subject of the toxaemia of pregnancy considers their structure. The physical basis of the disease is discounted. Just as happened in Alexandria after the disappearance of its first professors, so to-day the cry is, "To hell with anatomy."

Zip Fasteners

Dr. A. H. PRICE (Reading) writes: Some years ago while I was trout fishing, a man came down the little path and spoke to me, showing me his zip fastener (April 28, p. 948) entangled with his dewlap. Fortunately I had with me a very small but powerful wire-cutter that had lain in my creel. It took less than ten minutes to free the zip fastener, though indeed a few drops of blood were shed. Perhaps the purists would want to know why there was need of a wire-cutter, for large hooks; but salmon were about. Twice I have cut the wire of a hook, once in a man's upper lip and another time in an eyelid.

Dr. W. M. PENNY (Beckenham) writes: Is Captain H. Ellis's "Unusual Accident" (April 28, p. 948) so very infrequent? My patient also was a soldier, who at the end of his leave caught the dorsal surface of his prepuce in the zip. The fastener was snipped out and the wound closed. He was certified to be unfit to travel owing to a "minor operation." Young women who wear their corsets next to the skin may suffer a similar kind of accident.

Samples (and Pamphleteers)

Dr. R. ODDIE (London, S.W.3) writes: Your correspondent, Dr. D. Hanbury, of Midhurst (March 31, p. 704), has my sympathy; for, though I am literally "in the trade" myself, I too get many samples by post. But I must enter a modest plea in defence of what he calls the "pamphleteers" who write the accompanying advertisements. As an experienced but humble exponent of this art I can assure him that reliance on "exotic bibliographical references" as a means of enlisting professional interest in our wares is rarely called for nowadays. The doctor is too busy and had too much of it in the past. The function of the pamphleteer is largely *interpretative*: he tells the doctor—be it hoped clearly and concisely—what the commercial fraternity (and other doctors) are up to. Indeed, were it not for the medical departments of pharmaceutical manufacturers undertaking such functions, the busy general practitioner might frequently be ignorant of the practical value of new (as also of the fresh indications for old) remedies in his everyday work. In the past few months the rate of demand for a certain well-established proprietary drug has, following the issue of "pamphlets" suggesting its use in a new indication (for the symptomatic treatment of a certain infectious disease), increased twentyfold. It seems possible that a useful purpose has thereby been subserved for the benefit of doctor and patient. Were my erudition a match for the problem I would conclude, in Latin, "The proof of the pudding . . . Yours sincerely, The Cook."

Correction

Dr. F. Dudley Hart writes to point out that there was an error in the report of his address (April 21, p. 879), since the reference to Still should have been omitted.

Medical Notes in Parliament

National Health Service Bill

Lord HADEN-GUEST moved the second reading of the Bill in the House of Lords on May 9. He paid tribute to the "wonderful achievements" of the Service and briefly outlined the changes introduced in the Bill. Lord BALFOUR of INCHRYE said that on his side of the House they had no delight in the charges, but they accepted the Bill as a regrettable necessity brought about by a too hurried introduction of the full scheme before the professions, the hospitals, and the institutions were administratively ready. Lord AMULREE welcomed the clause providing for treatment abroad for tuberculosis patients, and said he felt sorry that it had been found necessary to depart from what had been a fine principle in the Act.

Lord WEBB-JOHNSON said that unless there was some charge for medicines and appliances there would be wanton waste. Lord FARINGDON believed that in the Bill there had been a serious sacrifice of principle, and feared that charges would have to be added for artificial limbs, hearing-aids, and so on; he deplored this "special tax" on those to whom fortune had been less kind. Lord HADEN-GUEST, winding up the debate, said that in helping to back up the national defence they were performing a service to the Health Service and to the nation. The Bill was then read a second and third time and passed.

On May 10 the Royal Assent was granted to the Bill.

X-ray Scheme for Miners

On May 7 Mr. E. H. C. LEATHER raised the subject of pneumoconiosis among miners and the proposed *x*-ray scheme. He paid tribute to the work of Dr. Fletcher and the Pneumoconiosis Board, and said that the important thing was to capitalize their work and make use of the knowledge they had acquired. This could be done, he maintained, only if the work was used as a preventive, and that meant the compulsory *x*-ray scheme he had been urging in the House for the past 12 months. If the disease was caught in the early stages when a man was only 5 or 10% affected, he could be removed to the surface and would be sound and fit like any other man. If the miners were forced to have a yearly *x*-ray examination both the psychological curse and a tremendous amount of human and economic waste would be eliminated.

Mr. HAROLD NEAL (Parliamentary Secretary to the Ministry of Fuel and Power) assured the House that the Government was deeply concerned with the problem of pneumoconiosis, and was dealing with the question of radiological examination as quickly as possible. The National Joint Pneumoconiosis Committee had for some time been considering a scheme of periodic examinations. It had decided that an experimental scheme was necessary before any general plan could be drawn up to cope with the "formidable objective" of examining more than half a million mine-workers. If the labour-saving and more easily operated mass miniature radiography was found to be sufficiently reliable to detect early pneumoconiosis, the introduction of the experimental scheme would be much easier than if large *x*-ray films had to be used. The experimental scheme would be confined to the routine detection of the disease and the safeguarding of the men they found to be infected.

Mr. Neal pointed out that under the Industrial Injuries Act every miner who feels that he might be suffering from the disease can make a claim for benefit, and then he is automatically given an *x*-ray examination. In the two and a half years ended December 31, about 31,000 *x*-ray films had been taken under this procedure, and during the same period 10,000 miners were diagnosed as having pneumoconiosis; all of them, whether or not they remained in the industry, were required to report for periodical re-examination. The increased confidence in the pneumoconiosis boards was shown by the fact that half of these

men remained in the coal-mining industry. The National Coal Board was taking all possible steps to eliminate the dust which caused the disease, and every effort would be made to remove pneumoconiosis from the mines.

On May 8 Mr. LEATHER moved that a Bill be brought in to allow compensation to be paid to workers who contracted pneumoconiosis as a result of their employment prior to July 5, 1948, and who were excluded from the then Workmen's Compensation Acts. Under these Acts a man was entitled to compensation only if he had served in the pits within the last five years, and Mr. Leather pointed out that a five-year time limit was unfair, because the disease may sometimes take as long as 20 years to become clear enough for diagnosis. He cited the case of a man in his constituency who left the pits 20 years ago when he was told he was suffering from chronic asthma, and who was not now entitled to any compensation because of the length of time he has been away from the mines. The Bill was read a first time and will be read again on June 22.

Dentists Act

Mr. BARNETT JANNER asked the Minister of Health on May 10 what was the present position about amendment of the Dentists Act. Mr. HILARY MARQUAND replied that proposals were under consideration, and that while it was not possible to introduce legislation in the present session it was the Government's intention to do so at an early opportunity.

Exports to China.—During the first three months of 1951 British exports to China included penicillin to the value of £4,000, iodides value £12,000, and other medicines and drugs value £8,000.

B.C.G. Vaccine.—Research into its use in Britain continues, but general distribution is not yet advisable.

Pay-beds.—There are 6,875 pay-beds in hospitals under the control of the Minister of Health, and on December 31 there were 1,190 patients on the waiting-list.

Medico-Legal

ANAESTHETIST FOUND NEGLIGENT

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

In a recent case a packer, Mr. Charles Alfred Fordyce, was awarded £400 damages for negligence[1] against the North-west Metropolitan Regional Hospital Board. He had also sued Mr. Neville Stidolph, the surgeon who had performed the operation in respect of which he complained, but during the course of the trial the jury found that there was no case of negligence against Mr. Stidolph, and a verdict was thereupon returned in his favour.

Mr. Fordyce's case was that on December 10, 1948, he was operated on for a duodenal ulcer in St. Mary's Hospital, Islington, for which the board was responsible under the National Health Service Act. During the operation the anaesthetist employed by the board injected curare into Mr. Fordyce's left arm to obtain muscular relaxation at the operation. It was said that in order to do this the arm was strapped above the patient's head, this manœuvre causing a lesion of the brachial plexus and affecting the nerves of his shoulder, with the result that, although the operation for duodenal ulcer was successful, Mr. Fordyce found when he recovered from the anaesthetic that his arm appeared to be paralysed.

The case for the board was that the anaesthetist, who was most experienced, having given more than 3,000 anaesthetics and having used curare more than 300 times, had not been negligent and that the arm was never strapped above Mr. Fordyce's head.

There was no suggestion that the anaesthetist had been negligent in selecting the arm for the curare injection.

The jury by their verdict found that the anaesthetist had been negligent and assessed the damages at £400. Mr. Justice Cassels adjourned the argument on the liability of the board upon the jury's finding, pending the judgment of the Court of Appeal in *Cassidy* v. *Ministry of Health*.[2]

On March 16, 1951, Mr. Justice Cassels, following the decision of the Court of Appeal, held that the board was liable in law for the anaesthetist's negligence, since the board was his employer. Accordingly he gave judgment against the board for £400 damages and costs.

ACTION AGAINST SURGEON WITHDRAWN

An action for negligence against Mr. Walter Galbraith in the Scottish Courts was recently[3] withdrawn by the pursuer, Mr. Malcolm Macfarlane, a master baker. Mr. Galbraith's action against Mr. Macfarlane for his fee in respect of the operation, which was the basis of Mr. Macfarlane's action, was also withdrawn after payment by Mr. Macfarlane of the fee.

Mr. Macfarlane had claimed £5,000 for alleged professional negligence. He alleged that he suffered from a serious abnormality of the shoulder which rendered it particularly susceptible to injury. In May, 1948, Mr. Galbraith operated on him for a diseased prostate, and that operation was entirely successful. Mr. Macfarlane complained that during the course of the operation he was tilted into such a position that pressure was put upon his shoulder. As a result the nerves were stretched, his hand was found to be paralysed next day, and had continued paralysed.

Mr. Galbraith's case was that he had taken all reasonable precautions for his patient's safety.

Lord Sorn had sent the action for trial by jury in spite of the absence of any averment on behalf of Mr. Macfarlane whether there was any alternative method of carrying out the operation, and if so what it was. Nor was there any averment in detail of what precautions could have been taken and in what respect the surgeon had failed to take them.

However, before the hearing before the jury was reached the action was withdrawn.

[1] *Manchester Guardian*, March 17.
[2] *British Medical Journal*, 1951, **1**, 480.
[3] *Glasgow Herald*, March 14.

Universities and Colleges

UNIVERSITY OF OXFORD

An examination for a Radcliffe Travelling Fellowship, of the annual value of £300 and tenable for two years, will be held during Hilary Term, 1952, at the University Museum. Full particulars may be obtained from the Regius Professor of Medicine, University Museum, Oxford, to whom applications must be sent by January 31, 1952.

The Board of the Faculty of Medicine will make an election, without examination, to the Schorstein Research Fellowship in Medical Science in June, 1952, if a candidate of sufficient merit offers himself. The Fellowship is of the value of £300 and will be tenable for one year from October 1, 1952. Candidates must submit their applications to the Secretary of the Medical School, University Museum, Oxford, by May 1, 1952.

Candidates for the Rolleston Memorial Prize, 1952, which is now of the value of about £90 and is awarded every two years, should submit their applications to the Head Clerk, University Registry, Oxford, before March 31, 1952.

Dr. Ian Wood will deliver a Litchfield Lecture on "Gastric Biopsy in the Study of Chronic Gastritis and Pernicious Anaemia" at the Radcliffe Infirmary, Oxford, on Wednesday, June 6, at 5 p.m.

UNIVERSITY OF CAMBRIDGE

Dr. M. G. P. Stoker has been reappointed Huddersfield Lecturer in Special Pathology from October 1 with tenure to the retiring age, and Dr. G. F. Roberts, Dr. B. M. Herbertson, and Dr. N. B. Finter have been reappointed University Demonstrators in Pathology, all with tenure for two years from October 1.

A University Lecturer and a University Demonstrator in the Department of Anatomy are to be appointed by the Appointments Committee of the Faculty of Biology "B." Full particulars may be obtained from the secretary of the committee, Mr. M. H. Gleeson-White, Department of Pathology, Tennis Court Road, Cambridge, to whom applications for the posts must be sent by June 6.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

At a meeting of the Council of the College, held on May 10, with Sir Cecil Wakeley, President, in the chair, A. H. Harkness, I. W. Magill, A. O. Parker, Surgeon Captain R. W. Higgins, R.N., and Professor T. Nicol were admitted to the Fellowship.

The Walker Prize was presented to Professor Alexander Haddow and the Begley Prize to Mr. G. L. Howe.

Professor Ernest Finch was re-elected to serve as the representative of the College on the Court of Governors of the University of Sheffield.

Diplomas of Membership were granted to the candidates whose names were printed in the report of the meeting of the Royal College of Physicians of London in the *Journal* of May 5 (p. 1025).

Diplomas were granted, jointly with the Royal College of Physicians of London, to the following successful candidates:

DIPLOMA IN CHILD HEALTH.—G. N. H. Cranswick, A. J. Watson.

DIPLOMA IN LARYNGOLOGY AND OTOLOGY.—Coroth M. Leelavathi.

DIPLOMA IN PUBLIC HEALTH.—H. L. Wolfe.

DIPLOMA IN TROPICAL MEDICINE AND HYGIENE.—R. M. Kapadia.

The following hospitals were recognized under paragraph 23 of the Fellowship regulations: North Lonsdale Hospital, Barrow in Furness (surgical registrar and house-surgeon (general), orthopaedic house-surgeon. All posts for six months only). Ipswich Borough General Hospital (two house-surgeons, for six months). West Norfolk and King's Lynn General Hospital (surgical registrar, for six months). Margate Hospital (surgical registrar, for six months). Ramsgate Hospital (surgical registrar, for six months). Southport General Infirmary (senior registrar).

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW

At a meeting of the Royal Faculty of Physicians and Surgeons of Glasgow held on May 7, with the President, Mr. Walter W. Galbraith, in the chair, the following were admitted Fellows of Faculty *qua* Physician: A. C. McDougall, M. B. Urs. B. McK. Dick was admitted a Fellow of Faculty *qua* Surgeon.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

The Diploma in Obstetrics has been awarded to the following successful candidates: E. A. Agius, A. S. Arneil, Janet M. Bell, D. G. B. Bennett, E. I. Boxer, H. S. Brown, J. A. C. Brown, C. B. Burdett-Smith, R. K. Burt, J. D. Chalmers, R. A. Chesterfield, Jeanne M. Clements, J. F. Connolly, J. S. Cox, T. I. Crichton, J. M. A. Critchley, Margaret E. Davies, J. A. Dew, A. J. Dinn, H. G. Dixon, D. C. Dymond, E. Evans, Harriet E. Faris, Margaret M. Farrell, Ethel A. Fisher, Hanora H. Forde, J. M. Frew, D. C. H. Garrod, H. S. Gavourin, N. N. Ghosh, H. J. Giwelb, N. G. O. Gourlay, M. Grant, K. Greig, P. Griffiths, H. Haigh, J. S. Happell, W. T. Harrett, J. W. S. Harris, Kathleen J. Harrison, Patricia E. Hartley, M. M. Herbert, G. J. S. Herdman, Ruth N. E. Hinckley, J. G. Inglis, W. G. Irwin, B. Isaacs, W. C. Jamieson, Dorothy M. Jennings, A. T. Johnson, A. W. Johnson, K.-M. Kawa, H. M. Kent, G. Kettlewell, H. M. Kirkpatrick, P.-C. Lai, Catherine M. Lamplugh, D. C. Langwell, Joyce H. Lazarus, J. J. Lee, W. Lees, T. P. Linehan, C. D. Linton, H. A. R. Loxdale, H. S. M'Callum, A. McCawley, D. P. McDermott, J. McDowall, Susanne M. MacGregor, W. J. M. Mackenzie, F. J. McKenna, L. P. Mackie, Cynthia J. McPherson, E. J. Mann, J. G. Mathie, B. Measday, Margaret L. Meikle, A. L. Mintz, Rhona E. Morgan, F. J. Mouser, Jessie M. B. Muirhead, Anne M. M. Oriel, E. Perelman, Evelyn Peters, Violet M. J. Procter, Margaret D. E. Quinet, E. J. H. Reford, A. M. Reid, D. H. Richards, J. H. Ridgwick, Freda M. Roberts, D. J. Rodger, I. P. Ross, M. Sackwood, I. N. Samuel, Joycelyn H. W. Sandison, Muriel J. Scudamore, H. Seid, P. N. Sinha, June M. Smith, P. M. Smith, Isobel M. W. Stark, R. G. O. Tayler, O. H. Taylor, E. Thomas, S. Thurairetnam, W. L. Timmins, E. L. Trott, A. C. Turnbull, Ethel M. Wallis, Alexandra C. Watson, Pamela L. C. Watson, Margaret L. Watt, Grace A. M. Webster, H. M. White, H. W. Wilson, M. B. Wingate, P. A. T. Wood, Frances M. E. Wylde.

Vital Statistics

Cattle Slaughtered for Tuberculosis

During January 1 to March 31 of this year the numbers of bovine animals slaughtered under the Tuberculosis Order of 1938 were as follows: England 947, Scotland 104, Wales 74; total 1,125 (Ministry of Agriculture and Fisheries). The numbers of bovine animals in the United Kingdom slaughtered under this Order in the last six years are shown in the following Table:

Year	Number Slaughtered
1945	9,633
1946	8,266
1947	6,545
1948	6,320
1949	5,813
1950	5,296

Deaths in the Large Towns

The number of deaths in the large towns has been considerably higher during the present year than in the corresponding period of 1950. In the second week of this year 10,328 deaths were registered, being 4,808 more than in the second week of 1950. The difference between the corresponding weeks of the two years gradually declined, but it was not until the ninth week that the difference fell below 1,000. For the past two weeks the number of deaths has approximated to the level of last year. During the first 17 weeks of this year 28,604 more deaths were registered in the great towns than in the first 17 weeks of 1950.

Road Accidents

Road casualties in Great Britain during March totalled 16,442, an increase of 2,837 compared with March, 1950. Of this total, 404 were killed, 4,027 seriously injured, and 12,011 slightly injured (Ministry of Transport). A disturbing feature of the March figures is that for the first time since the war they exceed the total for the last corresponding month before the war, March, 1939, which was 15,854. The increase is probably due to the fact that Easter this year fell in March, whereas in 1939 it was in April.

Health Records in Northern Ireland

According to a statement from the Registrar-General for Northern Ireland, the infant and maternal mortality rates in 1950 were the lowest ever recorded, and so also was the death rate from tuberculosis. The infant mortality rate decreased from 45 the previous year to 40 deaths per 1,000 live births. (In England and Wales it was 30.) The maternal mortality rate declined from 1.4 in 1949 to 1.2 per 1,000 live births. The death rate from tuberculosis was 48 per 100,000 population, which is one-third of the rate 25 years ago.

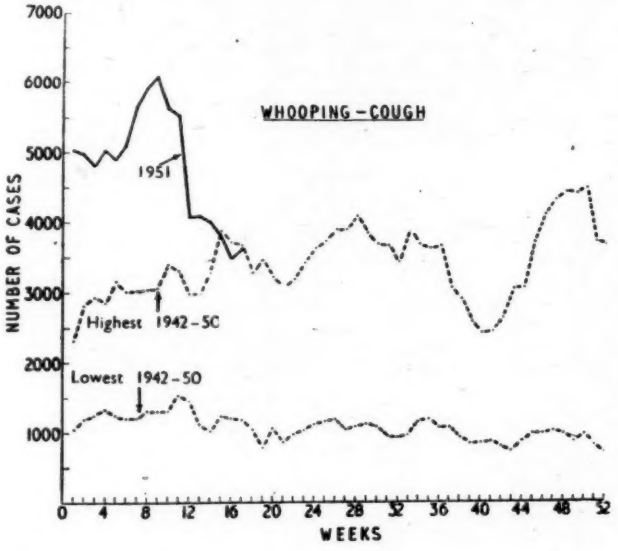
The birth rate fell from 21.4 in 1949 to 21 per 1,000 of the population in 1950. (In England and Wales it was 15.8.) The death rate was the same at 11.5. The death rate from cancer in 1950 was 150 per 100,000 population, against 115 in 1935. The rate has gradually increased, but the increase has slowed in the last seven years.

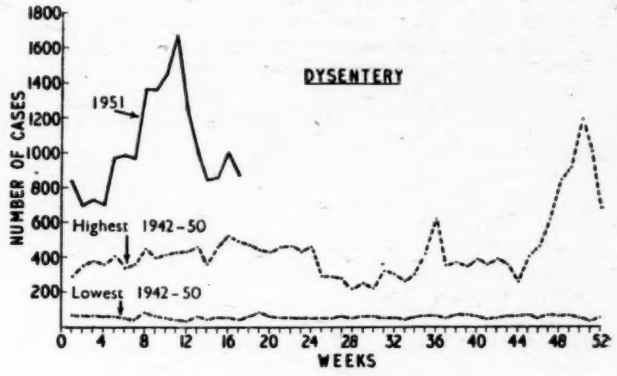
Week Ending May 5

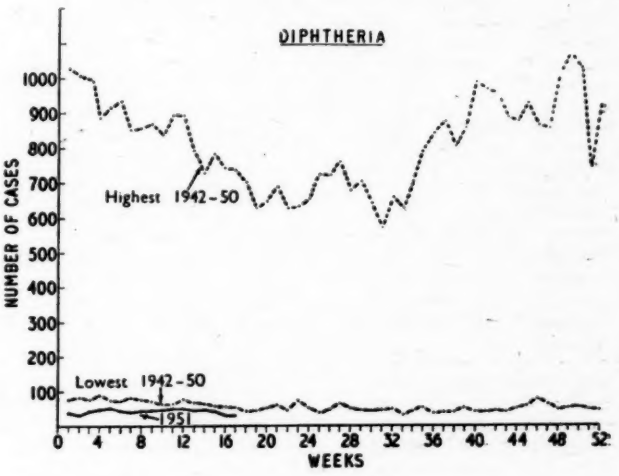
The notifications of infectious diseases in England and Wales during the week included: scarlet fever 1,032, whooping-cough 3,483, diphtheria 45, measles 18,310, acute pneumonia 588, acute poliomyelitis 21, dysentery 833, paratyphoid fever 7, typhoid fever 4. Deaths from influenza in the great towns numbered 10.

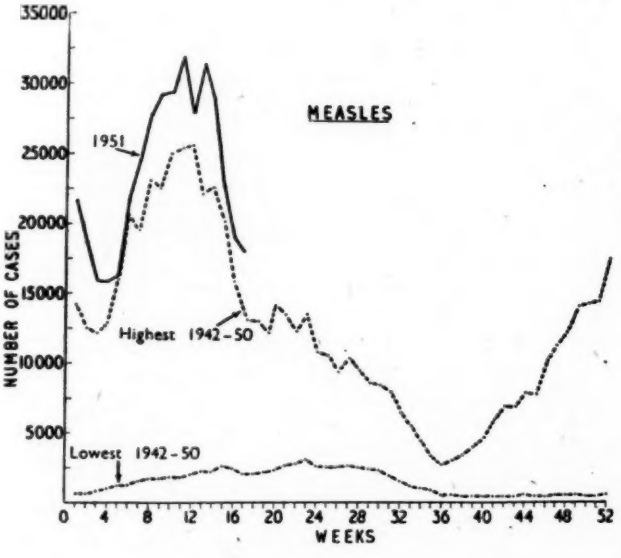
Graphs of Infectious Diseases

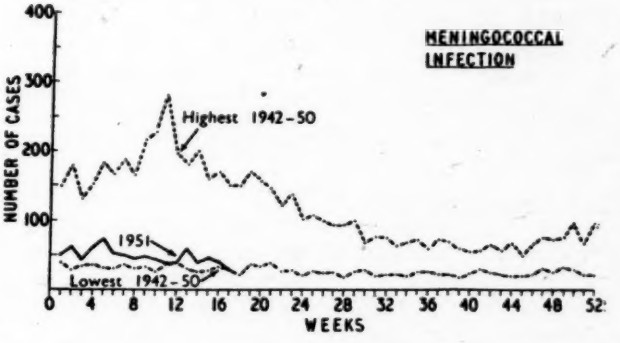
The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported during the nine years 1942–50 are shown thus - - - - - - -, the figures for 1951 thus ———. Except for the curves showing notifications in 1951, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.

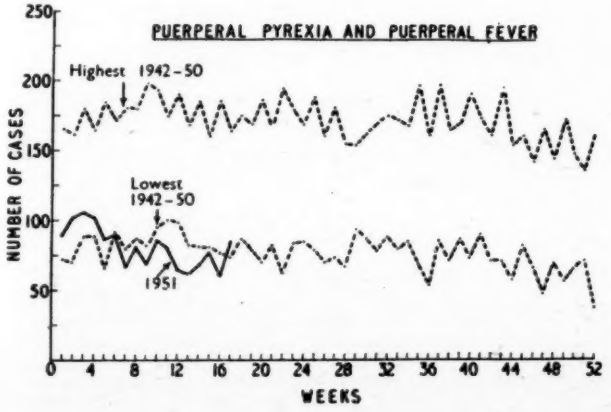












Infectious Diseases

In England and Wales during the week ending April 28 the number of notifications of whooping-cough rose by 145 and of scarlet fever by 136, while those of measles fell by 1,019 and dysentery by 131.

Only small changes occurred in the local trends of scarlet fever. The only large variation in the returns for whooping-cough was a rise of 42 in Lancashire. The largest falls in the number of notifications of measles were Yorkshire West Riding 462, Essex 219, Southampton 192, Surrey 102, while the largest rises were Cumberland 132, Lancashire 97, Warwickshire 75, and Kent 66. The chief feature of the returns of diphtheria was a rise of 7 in Yorkshire West Riding.

More than one case of acute poliomyelitis was notified in five counties, but the only administrative area with multiple cases was Birmingham C.B. 3. The largest returns for dysentery were London 136, Lancashire 122, Yorkshire West Riding 121, Middlesex 69. In Scotland the number of notifications of dysentery fell for the fourth consecutive week, and the total is now one-half of the value of a month ago. The largest centres of infection were the cities of Glasgow 36 and Edinburgh 16.

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles for the week ending April 28 (No. 17).

Figures of notified *cases* are for: (*a*) England and Wales (London included). (*b*) London (administrative county). (*c*) Scotland (*d*) Northern Ireland. (*e*) Eire. Figures of *births and deaths* and of *deaths* recorded under each disease are for: (*a*) The 126 great towns in England and Wales (London included). (*b*) London (administrative county). (*c*) The 16 principal towns in Scotland. (*d*) The 10 principal towns in Northern Ireland. (*e*) The 13 principal towns in Eire. A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, Northern Ireland, and Eire, the Ministry of Health and Local Government of Northern Ireland, and the Department of Health of Eire.

Disease	1951 Week Ending April 28					1950 Corresponding Week					1942–50 England & Wales Corresponding Week		
	(*a*)	(*b*)	(*c*)	(*d*)	(*e*)	(*a*)	(*b*)	(*c*)	(*d*)	(*e*)	Highest	Median	Lowest
Diphtheria	32	1	12	—	2	55	5	20	3	4	737	389	55
Deaths	—	—	—	—	—	1	—	—	—	—			
Dysentery	871	136	104	11	3	275	10	182	—	—	486	160	38
Deaths		—		—			—		—				
Encephalitis, acute	6	1	—	—		1	—	—	—	—	6	2	—
Deaths		—			—		—						
Erysipelas			15	6	2			26	3	6			
Food-poisoning	¶ 71	5		2		73	1		45				
Infective enteritis or diarrhoea under 2 years				18	24					11			
Deaths	12		2	—	3	16		3	—	—			
Measles*	18,006	1,017	482	226	151	6,380	203	612	276	110	13,204	7,962	2,025
Deaths		—	1	—	—			—	—	—			
Meningococcal infection	29	2	22	2	6	28	4	16	—	2	150	57	28
Deaths		—	1				—	2					
Ophthalmia neonatorum	45	1	8	—		45	3	8	2		100	62	44
Pneumonia, influenzal	570	34	8	3		548	23	7	10	—	909	647	453
Deaths (from influenza)†	13	1	—	1	—	32	7	—	—	3			
Pneumonia, primary			189					172					
Deaths	192	30		15	9	169	32		10	4			
Poliomyelitis, acute:													
Paralytic	11	—	2	—	3	26	2	7	—	1	26	7	3
Non-paralytic	8	1											
Deaths§	5	—			—	2	—			—			
Puerperal fever			3				—	12					
Puerperal pyrexia‖	85	8	12	2	3	74	6	10	—		164	136	74
Scarlet fever	1,084	87	143	32	80	1,124	77	163	67	69	1,764	1,124	785
Deaths		—	—	—	—			—	—	—			
Smallpox	—	—	—	—		—	—	—	—				
Deaths				—					—				
(1) Tuberculosis, respiratory			188	42				171	28				
(2) Tuberculosis, non-respiratory			38	9				37	11				
(1) Deaths	127	15	20	6	11	203	37	42	6	12			
(2) Deaths		8	3	1	6		1	4	—	3			
Typhoid fever	4	—	1	—	—	3	—	3	—	2			
Deaths¶	—	—	—	—		—	—	—	—	—			
Paratyphoid fever	4	—	—	—		7	—	—	—		23	10	6
Whooping-cough	3,643	248	555	50	58	3,276	144	428	47	103	3,684	2,044	1,190
Deaths	5	1	1	—	—	5	1	1	—	—			
Deaths (0–1 year)	230	32	44	11	22	236	40	35	10	11	468	339	236
Deaths (excluding stillbirths)	5,015	763	633	121	180	4,930	775	648	133	190	4,930	4,553	4,057
Annual death rate (per 1,000 persons living)			12·8					13·0					
Live births	7,190	1,141	956	232	457	7,322	1,168	1,038	260	402	10,148	7,798	6,312
Annual rate per 1,000 persons living								20·9					
Stillbirths	195	27	31			219	29	32			264	222	187
Rate per 1,000 total births (including stillborn)			31					30					

* Measles not notifiable in Scotland and returns are approximate. † Includes primary form for England and Wales, London, and N. Ireland. § The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, and London (administrative county), are combined. ‖ Includes puerperal fever for England and Wales and for Eire. ¶ Deaths from paratyphoid fever are combined with those from typhoid fever.

Medical News

Poliomyelitis Research

The Royal College of Physicians announces that a committee has been set up to provide those working on the aetiology, epidemiology, prevention, and treatment of poliomyelitis with opportunities for the exchange of information and the discussion of common problems. These workers will be encouraged to make recommendations. On April 21 the chairman of the Infantile Paralysis Fellowship, a lay society, speaking at a national conference at York, said that they also hoped to form a research organization which leading medical authorities would be invited to join.

Royal Victoria Infirmary, Newcastle

On May 23 the infirmary will celebrate the bicentenary of its foundation. Before 1751 there were only three or four physicians and about a dozen surgeons practising in Newcastle, which then had a population of 20,000. Even before the laying of the foundation stone in September, 1751, a house was taken in Gallowgate and opened in May, and seven in-patients were admitted. The house contained 33 beds, which were soon filled, making further accommodation necessary until the new infirmary was ready for patients in October two years later. The first physician was Dr. Adam Askew, and one of the early surgeons was William Hewson, a pupil of the Hunters, famed for his classical work on the lymphatics and on the blood. Among the eminent surgeons since connected with the infirmary was Rutherford Morison, whose enthusiasm for new methods was well known. In 1896 increasing demands on the infirmary made the building of a new hospital essential, and among those who subscribed were Mr. John Hall and Mr. J. C. Eno, who had started his career as a dispenser at the infirmary. The new Royal Victoria Infirmary was opened on July 11, 1906, by King Edward VII. The medical school was founded in 1834 as the Newcastle-upon-Tyne School of Medicine and Surgery; it became associated with the University of Durham in 1852 and in 1870 adopted the title of the University of Durham College of Medicine. The concentration of university and hospital teaching in one central group of buildings was completed when the Dental Department of the School was established in the grounds of the infirmary in 1931.

Faculty of Ophthalmologists

At the council meeting held on April 13 Mr. O. M. Duthie was elected president of the Faculty of Ophthalmologists for 1951–2, with Mr. R. C. Davenport and Mr. A. B. Nutt as vice-presidents. Mr. E. G. Mackie was elected honorary treasurer and Mr. J. H. Doggart honorary secretary.

Norwegian Drive against Tuberculosis

Nearly two-thirds of the Norwegian population have so far had *x*-ray examinations as part of Norway's latest campaign to intercept and cure tuberculosis at the earliest possible stage, according to a British United Press report. Seven mobile laboratories are touring rural districts and towns, and all services, including *x*-rays, medical examinations, and vaccinations, are free of charge. Two more mobile laboratories will soon be sent to the remote regions of Northern Norway. In addition, a former minesweeper, fitted with modern *x*-ray equipment, has been covering coastal regions. A similar vessel is now being fitted out to take the service to fishermen and farmers along the Norwegian coast. The present programme aims at regular examinations of every Norwegian at three-year intervals. During the past 55 years, deaths from tuberculosis in Norway have dropped from 30.9 per 10,000 population in 1896–1900 to only 3.8 per 10,000 in 1949. There was a big decrease in 1948 and 1949, when the death rate from tuberculosis was brought down from 5.15 to 3.8 per 10,000 population.

General Dental Council Proposed

Dr. E. W. Fish, presiding in London at the opening of the May session of the Dental Board of the United Kingdom, suggested that a general dental council should be formed, according to a report in *The Times*, May 10. He said that the National Health Service Act had placed increasing responsibilities upon the dental profession which made it more than ever necessary that it should be self-governing, responsible for its own standard of education, its own discipline, and its own registration. A spokesman of the General Medical Council explained afterwards that the Dental Board itself had no powers; it might make recommendations, but it was the G.M.C. which gave authority.

Chelsea Clinical Society

The annual dinner of the Chelsea Clinical Society, held in the South Kensington Hotel on May 8, was as usual a highly successful occasion. The guest of honour, who proposed the toast to the Society, was General Sir Ronald Adam, chairman of the British Council. He spoke of the enormous demand for knowledge which Britain can satisfy, knowledge about medicine, about nursing, and about medical equipment. One result of sending anaesthetists to lecture in Italy was a £500,000 order for anaesthetic apparatus. Mr. Geoffrey Parker, the president of the Society, made a modest reply. The health of the guests was proposed by Dr. N. MacManus, and in reply Lord Horder congratulated the Society on its adventurousness in its choice of speakers for meetings during the previous year. Speaking of the close link between medicine and the social state of the population, Lord Horder remarked that attempts to thrust welfare on the people without the help of experts was doomed to failure. That there should be redundancy on the lay side combined with elimination of the experts was tragic. Professor E. C. Dodds also replied for the guests. Mr. Parker then performed his last two presidential duties, the first to make a presentation to the retiring secretary of the Society, Mr. H. Paxton Baylis, and the second to inaugurate the new president, Dr. J. H. Dunn.

Wills

Dr. William Armstrong, of Cheltenham, left £60,548, and bequeathed £100 to the Royal Medical Benevolent Fund.

Dr. Septimus Sunderland, of Bexhill-on-Sea, left £127,529, and bequeathed £100 to the French Hospital, Shaftesbury Avenue, W.C.

COMING EVENTS

Osler Club Dinner

The annual dinner of the Osler Club will be held this year at the South Kensington Hotel on July 12, to celebrate the 102nd anniversary of Sir William Osler's birth. Mr. S. C. Roberts, Master of Pembroke College, Cambridge, will give the Oslerian Oration on "The Rev. James Beresford, a bookish, donnish figure, 1764–1840; author of *The Miseries of Human Life*." Details may be had from the Hon. Secretary, Dr. W. R. Bett, 11, The Avenue, Bedford Park, W.4.

Housing Conference

A conference organized by the Housing Centre Trust will be held at County Hall, S.E.1, June 6–8. On the last day the speakers will be Dr. I. G. Davies, medical officer of health, Leeds, and Dr. Charles Hill, M.P. All information about the conference, which is intended to provide an opportunity for free discussion of the immediate problems of housing, may be obtained from the secretary, The Housing Centre Trust, 13, Suffolk Street, Haymarket, S.W.1.

Summer Schools

"The Family: Mother and Child" will be the theme of a summer school sponsored by the British Social Biology Council to be held at the Cité Universitaire, Besançon, France, from July 31 to August 14. The cost is £27, and early application is advised. Another school will be held at Wadham College, Oxford, from August 20 to September 3 on "Social Biology and Health." The cost is £16 16s., and application should be made as early as possible to the British Social Biology Council, Tavistock House South, London, W.C.1.

International Congress of Clinical Pathology

The International Society of Clinical Pathology will hold an international congress in London from July 16 to 20. The sessions will be divided into four sections—Microbiology, Morbid Anatomy, Chemical Pathology, and Haematology. Programmes and full information may be obtained from the secretary-treasurer, Dr. W. H. McMenemey, Maida Vale Hospital for Nervous Diseases, London, W.9.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, London, W.C.—May 21, 5 p.m., *"The Treatment of Facial Paralysis,"* by Miss D. J. Collier.

INSTITUTE OF OPHTHALMOLOGY, Judd Street, London, W.C.—May 21, 5.30 p.m., *"Certain Congenital Ocular Palsies,"* by Mr. A. B. Nutt.

INSTITUTE OF PSYCHIATRY, Maudsley Hospital, Denmark Hill, London, S.E.—May 21, 5.30 p.m., lecture-demonstration by Dr. Denis Hill.

LEBANON HOSPITAL FOR MENTAL AND NERVOUS DISORDERS.—At Cora Hotel, Upper Woburn Place, London, W.C., May 21, 3 p.m., annual meeting. Speakers include Dr. J. C. Sawle Thomas, chairman of the Medical Committee.

UNIVERSITY COLLEGE, Physiology Theatre, Gower Street, London, W.C.—May 21, 5.30 p.m., *"The Nervous Control of Electric Organs,"* by Professor A. Fessard (Collège de France).

WEST LONDON MEDICO-CHIRURGICAL SOCIETY.—At Royal Society of Medicine, 1, Wimpole Street, London, W., May 21, 8.30 p.m., *"Over-Population,"* Cavendish Lecture by Rt. Rev. Lord Bishop of Birmingham, E. W. Barnes, D.D., Sc.D., F.R.S.

Tuesday

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—May 22, 5 p.m., *"The History of Dermatology,"* by Dr. R. M. B. MacKenna.

INSTITUTE OF OPHTHALMOLOGY, Judd Street, London, W.C.—May 22, 5.30 p.m., *"Vision in Conditions of Low Illumination,"* by Dr. Dorothy Campbell.

LONDON SCHOOL OF ECONOMICS AND POLITICAL SCIENCE, Houghton Street, Aldwych, W.C.—May 22, 5 p.m., Hobhouse Memorial Lecture by Professor Charles Singer.

LONDON UNIVERSITY.—At Westminster Medical School (Meyerstein Lecture Theatre), Horseferry Road, London, S.W., May 22, 5.30 p.m., *"The Surgery of the Biliary System,"* Special University Lecture by Professor Warren H. Cole (University of Illinois).

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—May 22, 3.45 p.m., *"Phase-Contrast Microscopy of Mouse Sarcomas,"* Imperial Cancer Research Fund Lecture by Dr. James Craigie.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—May 22, 5 p.m., *"Diplopia,"* by Dr. T. H. Whittington.

ST. MARY'S HOSPITAL MEDICAL SCHOOL: WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY, Paddington, London, W.—May 22, 5 p.m., *"Aspects of Immunity to Influenza,"* Almroth Wright Lecture by Dr. C. H. Andrewes, F.R.S.

UNIVERSITY COLLEGE, Physiology Theatre, Gower Street, London, W.C.—May 22, 5.30 p.m., *"The Muscle Spindle,"* by Professor A. Fessard (Collège de France).

WEST END HOSPITAL FOR NERVOUS DISEASES, 40, Marylebone Lane, London, W.—May 22, 2.30 p.m., *"Sciatic Pain,"* clinical demonstration in neurology by Dr. Colin Edwards.

Wednesday

EDINBURGH UNIVERSITY.—At Physiology Class Room, May 23, 5 p.m., *"The Renaissance Upheaval,"* by Dr. Douglas Guthrie.

INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—May 23, 5 p.m., *"Precancerous Conditions of the Skin,"* by Dr. H. Haber.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—May 23, 5.30 p.m., *"The Theory and Management of Squint,"* by Mr. R. P. Crick.

ROYAL MICROSCOPICAL SOCIETY, Tavistock House South, Tavistock Square, London, W.C.—May 23, 5.30 p.m., *"Histological Techniques for the Electron Microscope,"* by Mr. M. S. C. Birbeck, M.A.

Thursday

EDINBURGH UNIVERSITY, University New Buildings (Anatomy Theatre), Teviot Place, Edinburgh.—May 24, 5 p.m., *"Tuberculous Meningitis: Problems in Pathogenesis and Treatment,"* Honyman Gillespie Lecture by Dr. N. W. Horne.

INSTITUTE OF OPHTHALMOLOGY, Judd Street, London, W.C.—May 24, 5.30 p.m., *"Visual Attention,"* by Dr. F. A. Elliott.

LONDON JEWISH HOSPITAL MEDICAL SOCIETY.—At Medical Society of London, 11, Chandos Street, London, W., May 24, 3 p.m., *"Ocular Manifestations of General Disease,"* lecture-demonstration by Mr. Joseph Minton.

MEDICO-LEGAL SOCIETY.—At 26, Portland Place, London, W., May 24, 8.15 p.m., *"Medicine in Industry—Its Social Significance,"* by Dr. Leslie G. Norman.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—May 24, 5 p.m., *"The Myopathies in Ocular Practice,"* by Dr. S. Nevin.

ST. ANDREWS UNIVERSITY.—At Lecture Theatre, Materia Medica Department, Medical School, Small's Wynd, Dundee, May 24, 5 p.m., *"The Pigment Cells of the Body,"* by Professor J. D. Boyd.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, London, S.W.—May 24, 4.30 p.m., *"Neurology,"* lecture-demonstration by Dr. Denis Williams.

Friday

INSTITUTE OF DERMATOLOGY, Leicester Square, London, W.C.—May 25, 5.30 p.m., clinical demonstration by Dr. Brian Russell.

KENT AND CANTERBURY HOSPITAL, Canterbury.—May 25, 5 p.m., clinical meeting.

●ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS, 58, Queen Anne Street, London, W.—May 25, 5 p.m., *"Anuria in Obstetrics,"* William Blair-Bell Memorial Lecture by Professor H. L. Sheehan.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—May 25, 5 p.m., *"Uses of Thrombin and Fibrinogen in Ophthalmology,"* by Miss M. Savory.

Saturday

WEST MIDLANDS PHYSICIANS ASSOCIATION.—At North Staffordshire Royal Infirmary, Stoke-on-Trent, May 26, 11 a.m., second meeting. Morning: case presentations; afternoon: scientific communications.

APPOINTMENTS

CROYDON GROUP HOSPITAL MANAGEMENT COMMITTEE.—*Second House-physician, Croydon General Hospital*, K. Simpson, M.B., B.S. *Casualty Officers, Croydon General Hospital*, A. Magdi, M.B., Ch.B., and Ann Z. S. Tylko, M.D. *House-surgeon, Mayday Hospital*, M. Finegan, M.B., B.Ch. *Surgical Registrar, Mayday Hospital*, C. J. Windsor, M.B., F.R.C.S. *Resident Medical Officer, Purley Hospital*, J. Black, M.B., B.Ch., D.T.M. *Senior Obstetrical House Officer, St. Mary's Maternity Hospital*, M. D. Kochan, M.B., B.S.

EAST ANGLIAN REGIONAL HOSPITAL BOARD.—*Assistant Chest Physician, Cambridge Chest Clinic*, E. M. Cheffins, M.B., B.S. *Assistant Psychiatrist, St. Audry's Mental Hospital*, P. McCauley, M.B., B.Ch., D.P.M. *Orthopaedic Registrar, Peterborough and District Memorial Hospital*, K. L. Cleminson, M.B., B.S.

FRASER-JONES, JOHN, M.B., B.S., Resident Anaesthetist, Bradford Royal Infirmary.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Rostron.—On May 6, 1951, at Penquite, Lelant, near St. Ives, to Dr. Rosemary (formerly Arkwright) and Kenneth Rostron, a son.

Scott.—On May 5, 1951, at Whiston County Hospital, Prescot, Lancs, to Barbara, wife of Bertram Scott, F.R.C.S.Ed., a daughter—Meriel.

Wojcicki.—On April 8, 1951, at Penley Hall Hospital, near Wrexham, to Zofia, wife of Dr. H. M. Wojcicki, a son—Henryk Janusz.

MARRIAGES

Spalding—Falle.—On May 5, 1951, at St. Mary's, Bryanston Square, London, W., John Michael Kenneth Spalding, B.M., M.R.C.P., to Elizabeth de Carteret Falle, M.R.C.P., D.C.H.

Watson—Pollard.—On May 4, 1951, at Greyfriars Church, Port-of-Spain, Trinidad, British West Indies, H. Preston Watson, F.R.C.S.Ed., to Margaret Eileen Pollard.

DEATHS

Arnott.—On May 6, 1951, at the London Hospital, William Arnott, M.B., B.S., of 2, Roundsmead Avenue, Loughton, Essex, formerly of Barnoldswick and Oxford, aged 69.

Hawke-Genn.—On February 24, 1951, Bernard Hawke-Genn, M.B., Ch.B., of 139, Blackburn Road, Great Harwood, Blackburn, Lancs.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Dangers of Adrenaline Sprays in Asthma

Q.—*Asthmatics who rely on adrenaline inhalations often use more and more of the 1 in 1,000 solution, and then demand the 1 in 100 solution, and use increasing quantities of that. (a) What are the possible dangers of prolonged adrenaline therapy, with increasing dosages, in chronic asthmatics? (b) Have any fatal cases been reported after inhalation of adrenaline or self-administered injections of adrenaline?*

A.—(*a*) Too frequent use of an adrenaline spray leads to atony of the capillary vessels after the immediate constricting effect has worn off. The consequent engorgement of the bronchial mucosa may cause intensification of the asthma. American investigators have shown a higher mortality among chronic spray users than among asthmatics who do not use this form of symptomatic therapy. However, their figures cannot be taken entirely at their face value because the more severely affected patients are more likely to become chronic spray users. Local ulceration of the mucosa has been described. *Iso*propyl*nor*adrenaline in 1% solution is thought to be a more effective preparation for use in a spray than adrenaline itself, but is likely to have the same drawbacks.

(*b*) I am not aware of death in asthma having been attributed to the use of an adrenaline spray. Hemiplegia, and possibly death also, may result from the accidental injection of 1 in 1,000 adrenaline direct into a vein instead of into the subcutaneous tissues.

Before or After Meals?

Q.—*What is a good rule in deciding whether medicine should be taken before, with, or after meals? When does it make no difference?*

A.—Medicines taken before meals are more rapidly and more completely absorbed than if they are taken after. Thus the hypnotic action of a barbiturate is greater if taken on an empty stomach than on a full one. Medicines intended to stimulate appetite and a good flow of gastric juice are given before meals. Those intended to counteract hyperacidity are usually taken after meals.

Medicines which have an irritant action on the stomach are taken after meals because the food protects the stomach from their action—for example, preparations of iron are commonly taken after meals.

Purgatives which are intended to stimulate intestinal contractions are taken on an empty stomach.

Substances which do not depress appetite and are absorbed along the course of the intestine can be taken at any time.

Treatment of Primary Syphilis

Q.—*What is the best treatment for primary syphilis?*

A.—Penicillin is now the mainstay in the treatment of syphilis. It has been used successfully for eight years, during which period many schedules of treatment have been tried, some using penicillin alone, others in which a course is followed by one or more courses of arsenic and/or bismuth. Penicillin alone will cure most cases of early syphilis, but until those treated have been observed for a longer period than is at present possible two follow-up courses of bismuth should also be given. Some workers still combine bismuth therapy with neoarsphenamine, but the administration of this toxic drug is not recommended.

In sero-negative primary syphilis 2 ml. (600,000 units) of procaine penicillin in arachis oil with 2% aluminium monostearate is injected intramuscularly once daily for 10 days. In sero-positive primary and secondary cases the injections are continued for 15 days. Owing to the ease of its administration an aqueous suspension of procaine penicillin may be preferred by the busy general practitioner: the daily dosage recommended for this is 900,000 units. Aqueous solutions of penicillin G, either 60,000–100,000 units three-hourly or 600,000 units eight-hourly, can also be given, but at the present time most workers advocate, even for in-patients, the once-daily injection of procaine penicillin already described.

On completion of the penicillin course there follow 10 weekly injections of 0.3 g. of metallic bismuth (injectio bismuthi *B.P.*) given intramuscularly, and this course is repeated after a month's rest interval.

Immunity after Primary Infection with Tuberculosis: Its Relation to the Value of B.C.G.

Q.—*It is stated that the frequent existence of a healed primary complex in patients later dying from tuberculosis indicates that the first infection does not protect against progressive disease in later life. As I understand that B.C.G. vaccine works by providing such antibodies as would be produced by a primary complex, is it a safe assumption that any immunity is in fact afforded by this vaccine?*

A.—The degree of immunity left by a healed primary complex is not great; it can be broken down in genetically susceptible persons by superinfection and possibly by unfavourable environmental conditions. Infection with virulent tubercle bacilli often fails, therefore, to protect against subsequent superinfection and its clinical consequences. Since bacteriological experience has consistently shown that the degree of immunity against a given infection is related to the virulence of the infecting organism—provided it is not so virulent that it causes serious disease—it follows that the attenuated B.C.G. strain cannot afford a stronger immunity than that resulting from infection with virulent tubercle bacilli; in fact, it is probably less. It would be unjustifiable to expect B.C.G. vaccination to be of any further value after a primary infection has occurred, because the virulent tubercle bacilli introduced at that time, if they do not cause progressive disease, will give rise to a stronger immunity than that caused by the less virulent bacilli in the vaccinal strain. All that can be hoped for from B.C.G. is that it will prevent the primary infection from spreading and giving rise to clinical tuberculosis. Unless our present concepts are quite wrong, B.C.G. vaccination cannot have any effect on the main body of tuberculosis mortality in Great Britain, which results not from primary infection but from superinfection occurring at some later date.

Biochemical and Other Changes in Pregnancy

Q.—*I would like to know what changes take place (a) in red cell dimensions and (b) in blood electrolytes during normal pregnancy. Can you please include some references in your reply?*

A.—(*a*) There appear to be no striking alterations in red cell dimensions during normal pregnancy. A slight tendency for an increase in mean cell volume and a slightly increased anisocytosis have, however, been reported. A good deal of information and further references to the literature are to be found in the papers of F. H. Bethell (*J. Amer. med. Ass.*, 1936, **107**, 564) and of G. A. Elliott (*J. Obstet. Gynaec. Brit. Emp.*, 1944, **51**, 198).

(*b*) There is an extensive literature on the blood electrolytes in pregnancy. A good summary of this is to be found in Peters and van Slyke's *Quantitative Clinical Chemistry. Part I: Interpretation* (1946). Williams and Wilkins, Baltimore.

Trans-abdominal Migration of the Ovum

Q.—*A woman of 25 was recently operated on for an ectopic pregnancy. At the time of the operation it was found that the left ovary was the seat of a large endometrial cyst, and that there were other signs of endometriosis, so that in all she required to have both the right tube (for the ectopic) and the left ovary removed. What are her chances of conceiving, considering both the anatomical changes and the endometriosis? Are any plastic procedures possible?*

A.—Pregnancy is possible but, as is implied in the question, is not very probable. Endometrioma alone is associated with low fertility, and the anatomical arrangements now make pregnancy depend on a long internal migration of the ovum. In the event of pregnancy there is also an added risk of tubal implantation.

Unfortunately, no treatment is likely to improve the situation. An attempt to approximate the remaining ovary and tube by some sort of plastic operation is a theoretical possibility, but it is extremely doubtful whether it would improve the chances of successful pregnancy, and in the opinion of the writer it is not justified in the circumstances of this case.

Was it Suicide?

Q.—*If a man is found dead, hanging from a rope, how may one tell whether death occurred before suspension or as a result of it?*

A.—If the man had died as a result of the hanging the appearances of the body after death might indicate that he was alive when the hanging occurred. This would depend, however, upon the exact cause of death, for if vagal inhibition or sudden syncope was the terminal event then asphyxial signs might not be present. If, on the other hand, the cause of death was asphyxia then haemorrhages into the skin and conjunctivae above the level of the ligature impression would be of assistance; these would be present even if the neck had been broken, provided that the circulation had persisted afterwards. Vital changes at the site of constriction might also be evident. The presence or absence of a seminal discharge would not help.

Two important points must be mentioned. First, it is relatively easy to cause a post-mortem fracture of the neck, especially if the person has arthritis of the spine. Secondly, haemorrhage into the skin and conjunctivae can also occur in death from heart failure associated with, for example, coronary thrombosis. It is the presence of such haemorrhages above the line of constriction that is of significance.

Vitamin C and Allergic Rhinitis

Q.—*Have large doses of ascorbic acid (up to 1 g. daily) a place in the treatment of allergic rhinitis?*

A.—There appears to be no convincing evidence that massive doses of ascorbic acid have a therapeutic action in nasal allergy. They are sometimes given in an attempt to abort the common cold, but here again they seem no more successful than any other nostrum.

Obstinate Tapeworm

Q.—*I have failed four times with filix mas, four to five capsules of 15 minims (0.9 ml.), in expelling the head of a tapeworm. The patient weighs 8 stone (50.8 kg.). What alternative treatment is recommended?*

A.—The dose of liquid extract of filix mas might be increased, say, by a third. Preliminary preparation of the patient over a couple of days, by a light fluid diet and saline purgation, would probably be helpful, and a further saline purge should be given about an hour after the drug has been taken. Should the increased dose of filix mas fail, then tetrachlorethylene, 3 ml., should be tried after similar preparation of the patient.

MEDICINE IN BRITAIN IN THE FESTIVAL YEAR 1951

ITS ACHIEVEMENTS AND ITS FUTURE

As announced in previous issues of the *Journal*, a series of festival scientific meetings jointly organized by the British Medical Association and the Royal Society of Medicine will be held throughout June in the Barnes Hall, Royal Society of Medicine, 1, Wimpole Street, London, W.1.

A programme was published on May 5 (p. 1033) which, though provisional, was complete in almost every respect, but there have been several amendments, which are included in the programme below.

The main addition is a general-practitioner symposium on Wednesday, June 27, at 10 a.m., entitled "Reactions in General Practice to Scientific Advances," at which Dr. G. F. Abercrombie will take the chair. The following speakers will take part in the symposium: Mr. John Everidge, Dr. Wilfred Oakley, Dr. Guy Dain, and Dr. Lawrence Dulake.

While the subjects to be discussed should interest all doctors, many of the meetings have been arranged for general practitioners and others who have wide interests rather than for specialists in their own fields.

Authorities on their subjects will take part in the symposia. It is expected that these meetings will be somewhat informal, and the speakers have been invited to talk freely on the subject from their own particular viewpoint, expressing their opinions and experiences and giving an opportunity for discussion and questions.

Application for tickets should be made *as soon as possible* to the Joint Secretaries of Symposia, British Medical Association, B.M.A. House, Tavistock Square, W.C.1. A special application form was enclosed with the *British Medical Journal* of May 5 and copies of this form may be obtained from B.M.A. House. Accommodation is limited to 300 per meeting, and tickets will be issued in strict order of application.

A comprehensive brochure of the symposia may also be obtained on application to B.M.A. House.

Accommodation

It is regretted that it has been impossible to make arrangements for hotel accommodation for any members from a distance attending the scientific meetings, and it is hoped that members wishing to stay in London during this period will make their own arrangements for accommodation.

Car Parking

Car parking is extremely difficult in the vicinity of the Royal Society of Medicine, and especially so during the period of the Festival of Britain. There are a number of bombed sites near by, but these are usually full up by 9 a.m. and remain so for the rest of the day. Those coming by car would be wise to park in the outskirts of London and continue their journey by public transport. The nearest Underground stations are Great Portland Street, Oxford Circus, Bond Street, and Baker Street.

Festival Lecture

Sir Henry Dale, O.M., F.R.S., will deliver the Festival Lecture in the Great Hall, B.M.A. House, on Wednesday, June 20, at 6.30 p.m. His title is "Medicine Yesterday

and To-morrow." The chairman will be Lord Webb-Johnson, President of the Royal Society of Medicine.

This lecture is open to the lay public, as well as to the medical profession, and applications for tickets should be made as soon as possible to the Public Relations Officer, B.M.A. House, Tavistock Square, London, W.C.1.

FESTIVAL SCIENTIFIC MEETINGS

Summary of Symposia

JUNE

Date and Time	*Subject*	*Chairman*
Mon., 4; 2.00 ..	The Peripheral Nervous System	Sir Henry Dale
Wed., 6; 10.30 and 2.30	Otorhinolaryngology ..	Mr. W. M. Mollison
Thurs., 7; 2.15 ..	Antibiotics	Sir Alexander Fleming
Fri., 8; 4.00 ..	Vascular System (Clinical)	Sir John Parkinson
Mon., 11; 2.30	Ophthalmology	Dr. A. W. S. Sichel
Tues., 12; 10.30	Plastic Surgery	Sir Gordon Gordon-Taylor
2.00 ..	Plastic Surgery (cont.) ..	Sir James Paterson Ross
Thurs., 14; 2.00	Central Nervous System ..	Dr. W. Russell Brain
Fri., 15; 4.30 ..	Anaesthetics	Dr. I. W. Magill
Mon., 18; 10.00	Poliomyelitis	Dr. F. M. R. Walshe
2.15 ..	Endocrinology (Clinical) ..	Dr. R. D. Lawrence
Tues., 19; 10.00	The Decline of Infant Mortality	Sir Allen Daley
5.00 ..	Burns	Dr. L. Colebrook
Wed., 20; 10.00	Peptic Ulcer	Sir Henry Cohen
2.15 ..	Endocrinology (Experimental)	Dr. A. S. Parkes
Thurs., 21; 10.00	Nutrition and the B Vitamins	Lord Horder
2.00 ..	Neurosurgery	Sir Hugh Cairns
Fri., 22; 10.00	Cardiovascular Disease in an Ageing Population	Dr. J. H. Sheldon
2.15 ..	Orthopaedics	Mr. S. L. Higgs
Mon., 25; 10.00	Cortisone and A.C.T.H. ..	Professor G. R. Cameron
4.00 ..	Vascular System (Physiology)	Lord Horder
Tues., 26; 10.00	Diagnosis and Management of Early Mental Disorders	Dr. Desmond Curran
4.30 ..	Tropical Medicine	Sir Philip Manson-Bahr
Wed., 27; 10.00	Reactions in General Practice to Scientific Advances	Dr. G. F. Abercrombie
4.30 ..	Epidemiology	Dr. W. H. Bradley
Thurs., 28; 10.00	Carcinoma of the Lung ..	Mr. T. Holmes Sellors
2.15 ..	Thoracic Surgery	Mr. N. R. Barrett

JULY

Mon., 9; 4.00 ..	Odontology	Sir William Kelsey Fry

Application forms may be obtained from the Secretary, B.M.A. House, Tavistock Square, London, W.C.1.

PROGRAMME OF SYMPOSIA

Monday, June 4

2 p.m.—THE PERIPHERAL NERVOUS SYSTEM. *Chairman,* Sir HENRY DALE, O.M., G.B.E., M.D., F.R.S. Professor G. L. BROWN, Transmission in Sympathetic Ganglia; Dr. B. KATZ, The Response of the Motor End-plate to a Nerve Impulse; Dr. W. S. FELDBERG, Mechanisms of Neuromuscular Block; Professor J. H. BURN, The Relation of *Nor*adrenaline to Adrenaline; Professor J. Z. YOUNG, Determination of the Size of Nerve Fibres; Mr. H. J. SEDDON, Recent Advances in the Repair of Injured Nerves; Professor GRAHAM WEDDELL, The Anatomy of Pain Sensibility.

Wednesday, June 6

10.30 a.m.—OTORHINOLARYNGOLOGY. *Chairman,* W. M. MOLLISON, C.B.E., M.Ch. *Recent Advances in Otology.* (1) Hearing-aids: Dr. T. S. LITTLER, The Development of the Medresco Aid; Mr. J. OTTY, Clinical Experiences with the Medresco Aid; Mr. P. G. GRAY, The Medresco Aid in Use—Patients' Experiences. (2) Hearing Tests: Mr. C. S. HALLPIKE, The Clinical Tests of Cochlear Function, Recent Developments of Theory and Practice. (3) The Surgery of the Labyrinth, Mr. TERENCE CAWTHORNE.

2.30 p.m.—*Malignant Disease of the Upper Respiratory Passages.* Mr. F. C. W. CAPPS, Malignant Disease of the Nose and Paranasal Sinuses; Professor F. C. ORMEROD, Malignant Disease of the Nasopharynx and Oropharynx; Mr. V. E. NEGUS, Malignant Disease of the Pharyngo-larynx and Larynx; Dr. H. A. LUCAS, The Pathology of Malignant Disease of the Upper Respiratory Passages; Dr. GWEN HILTON and Mr. T. M. PROSSOR, The Radiotherapy of Malignant Disease of the Upper Respiratory Passages.

Thursday, June 7

2.15 p.m.—ANTIBIOTICS. *Chairman,* Professor Sir ALEXANDER FLEMING, F.R.C.S., F.R.S. Professor Sir HOWARD FLOREY, Some Observations on the Antimicrobial Products of Fungi and Bacteria; Dr. E. P. ABRAHAM, Some Chemical Aspects of Antibiotics from Fungi and Bacteria; Dr. E. LESTER SMITH, The Production of Antibiotics; Professor L. P. GARROD, Acquired Resistance to Antibiotics; Professor CLIFFORD WILSON, Clinical Evaluation of Antibiotic Therapy; Dr. G. L. M. MCELLIGOTT, Antibiotics in Venereal Disease; Professor ROBERT CRUICKSHANK, Antibiotics in Infectious Disease.

Friday, June 8

4 p.m.—THE VASCULAR SYSTEM (Clinical). *Chairman,* Sir JOHN PARKINSON, M.D. Sir JAMES LEARMONTH, Surgery of the Arteries; Professor J. MCMICHAEL, Cardiac Failure; Dr. R. T. GRANT, Wound Shock; Professor G. W. PICKERING, Essential Hypertension.

Monday, June 11

2.30 p.m.—OPHTHALMOLOGY. *Chairman,* A. W. S. SICHEL, M.D., D.O. (President-Elect, B.M.A., 1951–2). Dr. L. C. THOMSON, Colour Vision; Dr. W. A. H. RUSHTON, Electrophysiology of the Retina; Mr. B. W. RYCROFT, Corneal Grafts (with film); Mr. A. G. CROSS, Contact Lenses; Professor ARNOLD SORSBY, Genetics in Ophthalmology.

Tuesday, June 12

10.30 a.m.—PLASTIC SURGERY. *Chairman,* Sir GORDON GORDON-TAYLOR, K.B.E., M.S. Sir HAROLD GILLIES, General Review; Sir WILLIAM KELSEY FRY, The External Ear; Mr. RAINSFORD MOWLEM, Report on the Development of the Cancellous Chip Bone Graft.

2 p.m.—PLASTIC SURGERY (*cont.*). *Chairman,* Professor Sir JAMES PATERSON ROSS, K.C.V.O., M.S. Professor T. POMFRET KILNER, Congenital Clefts of the Lip and Palate; Sir ARCHIBALD MCINDOE, Reconstruction of the Burned Face; Mr. RAINSFORD MOWLEM and Mr. L. W. PLEWES, Orthoplastics in Industry.

Thursday, June 14

2 p.m.—THE CENTRAL NERVOUS SYSTEM. *Chairman,* W. RUSSELL BRAIN, D.M., P.R.C.P. Professor W. E. LE GROS CLARK, The Contribution of Anatomy to Problems of Sensory Discrimination; Professor E. G. T. LIDDELL, Stimulation of the Motor Cortex in Monkeys; Dr. F. M. R. WALSHE, Some Principles Governing the Interpretation of Experimental Studies of Cortical Function, with Special Reference to the Organization of Movements; Dr. GREY WALTER, The Physiology of Adaptive Behaviour.

Friday, June 15

4.30 p.m.—ANAESTHETICS. *Chairman,* I. W. MAGILL, C.V.O., M.B., D.A. Professor E. A. PASK, Research; Dr. JOHN GILLIES and Dr. G. E. H. ENDERBY, Controlled Circulation; Dr. CECIL GRAY, Relaxants; Dr. W. W. MUSHIN, Supplementary Agents; Dr. M. D. NOSWORTHY, Thoracic Surgery; Dr. A. I. PARRY BROWN, Cardiac Surgery.

Monday, June 18

10 a.m.—POLIOMYELITIS. *Chairman,* F. M. R. WALSHE, O.B.E., M.D., F.R.S. Dr. W. H. KELLEHER, The Management of the Early Stage of Poliomyelitis; Dr. D. MCALPINE, The Early Symptomatology of Poliomyelitis Virus Infection; Dr. F. O. MACCALLUM, Virus Infection; Dr. A. H. GALE, Poliomyelitis as an Epidemic Disease in England and Wales; Mr. H. J. SEDDON, Poliomyelitis, the Convalescent Stage.

2.15 p.m.—ENDOCRINOLOGY (Clinical). *Chairman*, R. D. LAWRENCE, M.D. Mr. L. R. BROSTER, Some Surgical Aspects of Endocrinology; Dr. R. D. LAWRENCE, Two Types of Diabetes—With and Without Blood-insulin; Dr. P. M. F. BISHOP, The Oestrogens: Their Clinical Use; Dr. LEONARD SIMPSON, Pituitary-Adrenal Hyperfunction.

Tuesday, June 19

10 a.m.—THE DECLINE OF INFANT MORTALITY. *Chairman*, Sir ALLEN DALEY, M.D., D.P.H. Sir JAMES SPENCE, Professor T. MCKEOWN, Professor T. N. JEFFCOATE, Dr. H. K. WALLER.

5 p.m.—BURNS. *Chairman*, LEONARD COLEBROOK, M.B., F.R.S. Dr. J. P. BULL, The Problem of Fluid Replacement; Dr. E. J. L. LOWBURY, The Control of Infection; Mr. DOUGLAS JACKSON, Physical Signs which Indicate the Need for Grafting; Dr. P. DALLAS ROSS, Early Skin-grafting; Mr. RAINSFORD MOWLEM, The Use of Homografts for Extensive Burns; Mr. A. B. WALLACE, The Exposure Method of Treating Burns.

Wednesday, June 20

10 a.m.—PEPTIC ULCER. *Chairman*, Professor Sir HENRY COHEN, M.D., F.R.C.P. Mr. NORMAN TANNER, The Surgeon's Viewpoint; Dr. F. AVERY JONES, The Physician's Viewpoint; Dr. COCHRANE SHANKS, Radiological Diagnosis; Dr. HENRY WILSON, Pyschological Factors.

2.15 p.m.—EXPERIMENTAL ENDOCRINOLOGY. *Chairman*, A. S. PARKES, D.Sc., F.R.S. Professor E. C. DODDS, Synthetic Oestrogens; Professor F. G. YOUNG, The Endocrine Approach to the Problem of Diabetes; Dr. G. W. HARRIS, The Hypothalamo-Hypophysial Link in the Stress Syndrome; Professor E. B. VERNEY, The Excretion of Water and its Physiological Regulation; Dr. S. J. FOLLEY, Endocrine Factors in Lactation.

Thursday, June 21

10 a.m.—NUTRITION AND THE B VITAMINS. *Chairman*, Lord HORDER, G.C.V.O., M.D. Dr. LESTER SMITH and Dr. BODLEY SCOTT, The Treatment of the Macrocytic Anaemias, Professor B. S. PLATT; B Deficiencies in the Tropics; Dr. R. A. PETERS, The Clinical Implications of Research on Vitamin B_1; Dr. L. J. HARRIS, Nicotinamide and Pellagra.

2 p.m.—NEUROSURGERY. *Chairman*, Professor Sir HUGH CAIRNS, K.B.E., F.R.C.S. Professor N. M. DOTT and Mr. G. L. ALEXANDER, Intracranial Aneurysmal Malformations; Professor Sir GEOFFREY JEFFERSON, The Frontal Lobe; Professor Sir HUGH CAIRNS, Head Injuries; Mr. J. B. PENNYBACKER, Abscess of the Brain; Mr. HARVEY JACKSON, Tumours of the Orbit; Dr. L. GUTTMANN, The Care of the Paraplegic Patient.

Friday, June 22

10 a.m.—THE PROBLEMS OF CARDIOVASCULAR DISEASE IN AN AGEING POPULATION. *Chairman*, J. H. SHELDON, M.D., F.R.C.P. Professor A. M. BOYD, The Diagnosis and Management of Circulatory Deficiency due to Degenerative Arterial Disease; Dr. WILLIAM EVANS, Cardiac Pain. Other speaker Dr. T. ROWLAND HILL.

2.15 p.m.—ORTHOPAEDICS. *Chairman*, S. L. HIGGS, F.R.C.S., President, British Orthopaedic Association. Sir HARRY PLATT, Unusual Malignant Tumours of Bone; Sir GORDON GORDON-TAYLOR, The Surgery of Malignant Disease in the Vicinity of the Hip-joint; Sir THOMAS FAIRBANK, Some General Affections of the Skeleton; Mr. BRYAN MCFARLAND, Developmental Defects of Long Bones.

Monday, June 25

10 a.m.—CORTISONE AND A.C.T.H. *Chairman*, Professor G. R. CAMERON, F.R.C.P., F.R.S. Dr. G. W. HARRIS, The Clinical Implications of Recent Research Work on the Pituitary and Adrenal Glands; Dr. W. S. C. COPEMAN and Dr. OSWALD SAVAGE, The Rheumatic Diseases; Dr. D. LONG, Cortisone and Allergy; Dr. F. T. G. PRUNTY, Effects of A.C.T.H. and Cortisone in Acute Disseminated Lupus Erythematosus and Dermatomyositis; Professor HENRY MOORE, Experiences with Cortisone in Dublin.

4 p.m.—THE PHYSIOLOGY OF THE VASCULAR SYSTEM. *Chairman*, Lord HORDER, G.C.V.O., M.D. Professor K. J. FRANKLIN, The Change-over in the Circulation During and Shortly After Birth; Professor I. DE BURGH DALY, The Pulmonary Circulation; Dr. D. A. MCDONALD and Dr. J. M. POTTER, Some Remarks on Circulatory Rheology, with the Following Films: (*a*) Blood Streams in the Basilar Artery, (*b*) Velocity of the Blood Flow in the Basilar Artery; Professor J. TRUETA, The Renal Circulation; Professor H. BARCROFT, The Action of Adrenaline and *Nor*adrenaline on the Human Circulation.

Tuesday, June 26

10 a.m.—THE DIAGNOSIS AND MANAGEMENT OF EARLY MENTAL DISORDERS. *Chairman*, DESMOND CURRAN, F.R.C.P., D.P.M. Dr. NOEL HARRIS, The Psychiatrist's Viewpoint; Dr. THOMAS BEATON, The Mental Hospital in Relation to the General Public; Dr. KENNETH CAMERON, The Child Psychiatrist's Viewpoint.

4.30 p.m.—TROPICAL MEDICINE. *Chairman*, Sir PHILIP MANSON-BAHR, C.M.G., F.R.C.P. Professor H. E. SHORTT, Protozoology and World Economic Problems; Professor B. G. MAEGRAITH, Physiological Approach to Tropical Medicine; Sir NEIL HAMILTON FAIRLEY, Chemotherapy in the Control and Treatment of Malaria.

Wednesday, June 27

10 a.m.—REACTIONS IN GENERAL PRACTICE TO SCIENTIFIC ADVANCES. *Chairman*, G. F. ABERCROMBIE, M.D. *Speakers*: Mr. JOHN EVERIDGE, Dr. H. GUY DAIN, Dr. LAWRENCE DULAKE, Dr. WILFRED OAKLEY.

4.30 p.m.—EPIDEMIOLOGY. *Chairman*, W. H. BRADLEY, D.M. Dr. C. H. ANDREWES, Influenza and the Common Cold; Dr. W. N. PICKLES, Virus Diseases in General Practice.

Thursday, June 28

10 a.m.—CARCINOMA OF THE LUNG. *Chairman*, T. HOLMES SELLORS, M.Ch. Mr. R. C. BROCK, Professor D. W. SMITHERS, Dr. N. LLOYD RUSBY, Dr. W. R. S. DOLL.

2.15 p.m.—THORACIC SURGERY. *Chairman*, N. R. BARRETT, M.Ch. Mr. P. R. ALLISON, The Anatomy and Physiology of the Oesophagogastric Junction in Relation to Hiatal Hernia and Oesophageal Ulceration; Mr. C. PRICE THOMAS, The Surgery of Adenoma of the Bronchus; Mr. R. C. BROCK, Intracardiac Surgery.

Monday, July 9

4 p.m.—ODONTOLOGY. *Chairman*, Sir WILLIAM KELSEY FRY, C.B.E., M.D.S., F.D.S. *The Significance of Dental Sepsis to the Physician, the Ear, Nose, and Throat Surgeon, the Ophthalmologist, and the Dermatologist.* The Physician, Dr. A. H. DOUTHWAITE; The Ear, Nose, and Throat Surgeon, Mr. C. GILL-CAREY; The Ophthalmologist, Mr. J. H. DOGGART; The Dermatologist, Dr. W. J. O'DONOVAN. The subsequent discussion will be opened by Dr. WILFRED FISH and Professor MARTIN RUSHTON.

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